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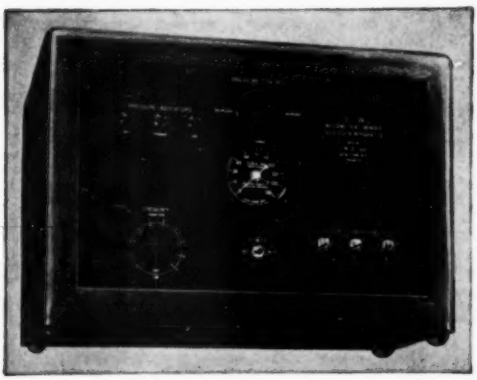

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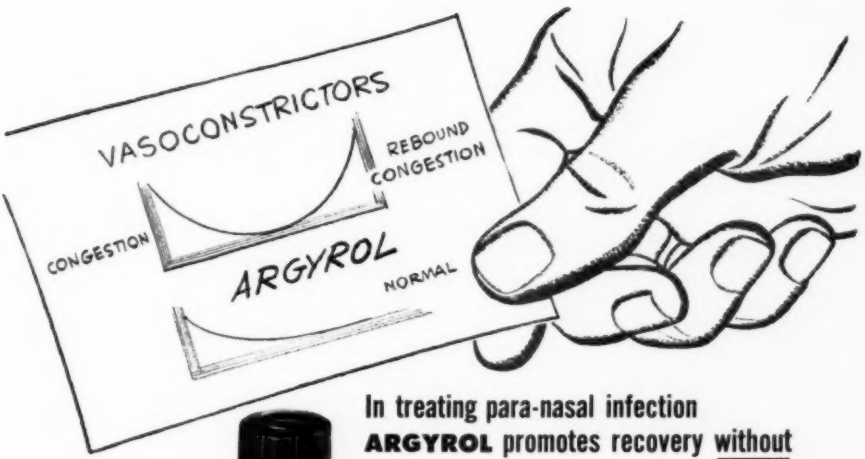

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ROBERT L. CRAIG, *Editor*

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BULLETIN OF
THE NEW YORK ACADEMY
OF MEDICINE

VOL. 28, NO. 2 FEBRUARY 1952

THE ELECTROCARDIOGRAPHIC EFFECTS OF MYOCARDIAL AND PERICARDIAL INJURY*

CHARLES E. KOSSMANN

Associate Professor of Medicine, New York University College of Medicine

"It is probable that [the string galvanometer] will give information of much value where the action of the heart, as a whole, is perfectly regular, and where the contraction, originating at the normal site of impulse formation, namely the sino-auricular node, progresses at normal rates through the heart and along definite and recognized channels."

This prophecy, from a paper by Lewis and Gilder,[1] was made in 1912 after the authors concluded that the "new chapter in clinical medicine" which resulted from the use of the instrument in "deciphering" irregularities of the ventricles and disorders "in the sequence of contraction in its chambers" was rapidly closing.

The prophecy has been amply born out in the four decades since it was made. Lewis had in mind the modifications in the electrocardio-

* Presented at the 24th Graduate Fortnight of The New York Academy of Medicine, Oct. 18, 1951.
From the Department of Medicine, New York University College of Medicine, the Adult Cardiac Clinic, Third (N.Y.U.) Medical Division, Bellevue Hospital, and the Cardiovascular Service and Clinic, Lenox Hill Hospital, N. Y.
Original investigations quoted were aided by grants from the New York Heart Association and the Knapp Foundation.

gram which he recognized to occur with hypertrophy. He lived long enough to see the string galvanometer give much more valuable information than his earliest observations made him suspect it would.

A great many investigations have contributed to the present-day understanding of the alterations in the electrical behavior of the myocardium which are reflected in recognizable modifications of the electrocardiogram. The most significant of these have been the studies, almost exclusively by F. N. Wilson and his school,[2] on the laws governing the behavior of an electromotive force in a volume conductor. The results of these original studies have been modified only slightly by subsequent investigations. Only a few problems remain to be solved in this area. If the year 1912 was regarded as the end of the era of the arrhythmias, the mid-twentieth century may be regarded as the time when the chapter on the effects of the body regarded as a volume conductor may be considered to be coming to a close.

A discernible third period, already well along, and destined almost certainly to have clinical repercussions, is concerned with the intensive study of the source of the electromotive force itself, namely the myocardial cell. Because an understanding of the electrical behavior of the cell is fundamental to an understanding of the electrocardiographic effects of myocardial and pericardial injury seen clinically, a resume of pertinent facts will be given.

The Cell

To begin with it is customary to accept Bernstein's membrane theory,[3] proof of which, with some modifications from the original, is convincing. The theory states that the resting cell possesses a membrane which is semipermeable to ions. These are oriented in such a way that the outside of the resting cell is electrically positive and the inside negative with reference to ground potential.

The difference in potential across the membrane has been measured in the squid giant axon,[4, 5] and in the sartorius muscle[6, 7] and the myocardial cell of the frog.[8] In these tissues it averages 45 to 88 mv. It is called the "resting membrane potential."

When the cell undergoes stimulation, natural or artificial, depolarization of the membrane occurs presumably due to a change in permeability to ions or other charged particles. The original potential not only disappears but reverses slightly (about 30 per cent) so that the membrane potential is temporarily opposite in polarity, but in less degree,

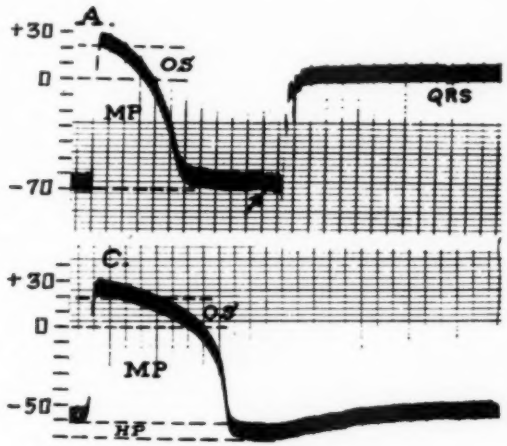

Figure 1—Action potentials of single cardiac ventricular fibers. (M.P. Resting membrane potential, O.S. Overshoot, HP Hyperpolarization.) All measurements made from bottom of string shadow. Ordinates—millivolts; abscissae—time. Vertical lines 0.1 second apart.

A. Action potential of single ventricular fiber. Arrow indicates start of withdrawal of electrode from cell to show return of string to zero value and presence of small surface electrocardiogram (QRS).

C. Action potential of longer duration.

(Woodbury, Woodbury, and Hecht, *Circulation* 1:264, 1950).

to the resting state. It is very probable that this "overshoot," as it is called, is comparable to the phenomenon of the same name known to occur in electrical condensers, and may be due to inductance[4] with a temporary realignment of electrons on the membrane, the reverse of what is found in the resting state.

Following the rapid depolarization there is a gradual restoration of the original membrane potential with varying speeds as shown in the varying slopes of the recovery curve. Sometimes there is at the end of recovery a slightly greater negative potential than before. This is temporary and is spoken of as "hyperpolarization."[9]

These collective phenomena, known as the "membrane action potential" are shown as they occur in the myocardial cell of a frog in Figure 1 taken from the paper by Woodbury, Woodbury, and Hecht.[9] Part A of this figure shows a membrane potential in the myocardial cell of a frog of 70 mv. As excitation proceeds over the cell there is an

overshoot of 30 mv with a gradual return to the original large negative potential as the repolarization proceeds slowly at first, more rapidly toward the end of systole. This part of the figure also shows the disappearance of the negative intracellular potential as the electrode is withdrawn from the cell, after which it is close to the surface of the heart and records a small ventricular complex (QRS) or "axial current."[10, 11] Part C shows a slower slope to repolarization and a drop of potential below its original intracellular level or "hyperpolarization."

It is noteworthy, for its clinical interest, that temperature has little effect on the voltage of the membrane action potential but the rate of depolarization is quite sensitive to this variable, being longer the lower the temperature.[8, 12]

From these remarks it is clear then that the action potential of the cell may be, if desired, divided into at least five phases: 1) depolarization, also called excitation, accession, or invasion, which represents a period of increasing activity of the cell; 2) overshoot, which is probably a condensation phenomenon on the membrane; 3) complete activity or possession partly obscured in direct cellular experiments by the gradual "leaking off" of the overshoot; 4) repolarization, also called recovery, regression, or retreat, which represents a period of decreasing activity of the cell; 5) hyperpolarization. The overshoot and the hyperpolarization may not be essential parts of the electrical process. In any case they may, for didactic purposes, be disregarded temporarily and the electrical activity of the cell defined as a tripartite one, consisting of accession, possession, and regression.[13]

The Conducting Medium

The relatively simple monophasic curve obtained during the study of the membrane action potential of a cell is altered when the electrode used to record it is moved to the exterior of the cell, and is separated from it by part of the physiological conducting medium. Analysis of the effects are possible because the accession process or period of increasing activity of the cell behaves as though it were a dipole or double electric layer with the positive pole or side facing the direction of excitation of the muscle. This results from the fact that with activity, as already shown, the polarity of the cell membrane decreases. Another way of saying this is that the density of charges on it is decreased. The resting muscle just ahead of the active muscle, being more densely polarized, behaves as though it were positive electrically with respect

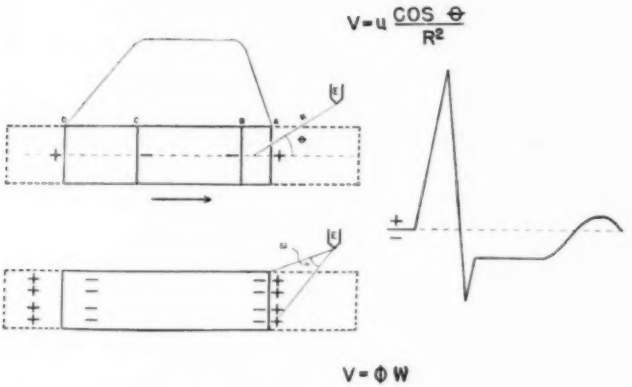

Figure 2—Methods of analyzing the effect of the membrane action potential on a unipolar lead in a homogeneous conducting medium.

The cell is shown diagrammatically twice, with the source of electrical energy in depolarization (AB) and repolarization (CD) being regarded as a dipole in the upper figure, and as a charged surface or lamina (double electric layer) in the lower figure. In the former the potential of the electrode, E, is defined by the upper formula in which μ is a constant which depends on the distance between the dipoles and the quantity of charge they carry, R is the distance from the center of the dipole to the electrode E, and θ is the angle between R and the positive side of the axis. In the latter the potential, V, of the electrode, E, is defined by the lower formula in which ϕ is a value which depends on the density of the charges on the membrane and ω is a solid angle subtended on a sphere of unit radius about E. Polarity of the electrode is determined by the side of the charged membrane seen by an observer stationed at E.

On the upper cell is drawn the membrane action potential as recorded in Fig. 1, with the omission of the overshoot and the negative after-potential (hyperpolarization). The diagrammatic electrogram on the right is the record obtained by the electrode in the conducting medium as a result of the changes in the electrical field of the medium brought about by the membrane action potential. The inequality of the positive and negative phases of this quadriphasic curve is ascribed to the special circumstance of the recording electrode being at the end of the cell opposite the point of stimulation.

to the active portion. The regression process or period of decreasing activity may be regarded similarly but with the polarity reversed since the active muscle precedes the resting muscle. Under such circumstances, provided the medium is homogeneous,[2] the effects of the dipole or double electric layer on an electrode or point in the medium may be analyzed by the formulae and diagrams in Figure 2. From the upper formula and diagram, it is clear that the potential (or size of the deflection in the finished record) will be larger the closer the dipole is to the point of recording (the shorter the distance, R). Also an elementary knowledge of trigonometry will make it obvious that as the

angle θ approaches o degrees, the effect on the electrode, E, in the conducting medium will be maximum and positive. At 180 degrees it will be maximum and negative. In the lower part of the figure, the effect of the charged membrane or double electric layer on electrode E will be greater as the area of the membrane is larger, and the distance between it and the electrode is smaller. These two variables are measured by the angle ω which is a solid angle subtended on a sphere of unit radius drawn about the point (E in figure) in the conducting medium being studied. The value, $\emptyset$, is determined by the number and the magnitude of the charges on the membrane.

The dipole or the double electric layer may be represented by a vector with an axis parallel to the axis of the dipole, or normal to the surface of the charged membrane. Its length is made proportional to the size of the electromotive force involved.

With either of these methods of analysis, then, the simple intracellular monophasic curve is converted into a more complicated extracellular, quadriphasic curve, as shown in Figure 2, where accession and regression are regarded as dipoles (upper figure) or double electric layers (lower figure). The asymmetry of the accession deflections (QRS) and the regression deflections (S-T and T) as shown in the figure is attributable to the special circumstance that the electrode in this instance is placed at the distal end of the strip. These two sets of deflections would be symmetrical if the lead was made from the middle of the strip.[13]

In a lead from the medium surrounding the isolated strip of muscle the processes of accession and of regression are equivalent. Although the latter process takes longer, the voltages involved are less, and the product of the two (time x voltage) is identical with, though opposite in sign, to a similar product for accession. This is the same as saying that the area of QRS is equal to the area of the T wave, and that the sum of the two is zero. In the electrocardiogram of the normal human ventricle the area of QRST is not equal to zero because certain variables are operative which delay the regression process in various regions of the ventricular muscle,[14] more particularly the subendocardial regions.[15] These differences in duration of the excited state are accurately measured by the area of QRST which, when reduced to a quadrential vector, indicates the direction and magnitude of these differences. Its direction is from an area where recovery is longest to an area where it is shortest. It is known as the ventricular gradient.

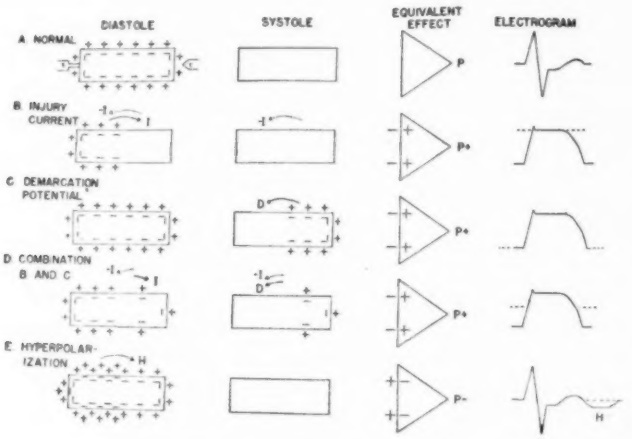

Figure 3—Some of the theoretical types of injury which may modify the electrical behavior of the cell. The equivalent effect is shown as the effect of a simple charged membrane or lamina on a point, P, in a surrounding conducting medium according to the formula $V = \phi\omega$ (see Fig. 2 and text). The electrograms display the phase in which the effect will be manifest, and its nature. E, electrode; S, stimulator; I, injury current; $-I$ compensating current; D, demarcation current; H, hyperpolarization.

Specific Electrical Effects of Injury

In any discussion of the effects of myocardial and pericardial injury on the electrocardiogram, there is one explanation which must be made at the outset, namely the definition of the word "injury." The term, as applied to the myocardium, is used loosely and a concept of its meaning will depend largely on whether one is a clinician, pathologist, embryologist, or microbiologist. For the purposes of this discussion, injury may be regarded as any process which either completely abolishes or only modifies, singly or in combination, the rate, course, or extent of the cellular processes of depolarization and repolarization.

Preliminary to this discussion, too, it is desirable to note that the total electrical effect of a resting cell on a point in a surrounding medium is zero (Fig. 3A) because this "double layer," being completely closed, has no boundaries. The solid angle subtended by it on a point in the surrounding medium is really the sum of two identical solid angles subtended by the same imaginary boundary but of opposite sign. The

sum of these and the potential of all points in the medium are obviously zero.[2, 16, 17]

Having some knowledge of what happens in the normal cell during electrical activity, the problem to be considered logically is how does injury, as defined, modify these processes.

The answer appears to depend largely on the degree of injury. The easiest degree to understand is the injury which results in complete functional and usually anatomic destruction of the cell. Such a cell no longer contributes an electromotive force of any kind. Its absence is reflected in the clinical electrocardiogram by changes in the initial ventricular deflections, QRS, since the dead cells no longer contribute to the mean manifest potential of ventricular depolarization which these deflections reflect. Since clinical death of myocardium is frequently extensive, the absence of the cells results in either the left arm or left leg becoming in effect a total or partial semidirect lead from the cavity of the left ventricle whereas normally they are semidirect leads from the surface of that chamber. An initial negative potential results which manifests itself as a Q wave in the unipolar lead from either or both extremities or in the bipolar leads (I, II, III) in which these extremities are used. The principles also apply to the precordial leads.[17-19]

The lesser degrees of injury are more complex, and knowledge of the basic electrophysiology concerned is still incomplete. However, an attempt can be made to classify what is known with the full realization that some of it is tentative depending on further investigations.

In addition to the type of injury which modifies QRS, there are at least six additional types which are reflected electrocardiographically in abnormalities of the S-T segment, the T wave, and perhaps the U wave. In discussing these, reference to the changes in a single cell will be made for the sake of simplicity. It is clear, however, that the discussion also applies to any aggregate of cells.

The best understood of these injuries is one which results in partial or complete depolarization of a part of the cell. The resting membrane potential in the injured area is of lesser magnitude, and hence this injured part is electrically negative with respect to uninjured parts (Fig. 3B). During diastole a current flows from the uninjured to the injured region known as the current of injury (I). The electrical effect is equivalent to a double electric layer with the negative side toward the injured region.[2] Since it is assumed to be constant, and may, for purposes of discussion be regarded as balanced by a compensating

current from the galvanometric circuit (-I in Fig. 3B), the current involved causes no discernible deflection of the galvanometric recorder during diastole. But if the entire cell should be abruptly depolarized by normal activity, the recorder will deflect during systole to a degree proportional to the magnitude of the original current of injury, and in a direction determined by the location of the electrode with respect to the injured and uninjured regions. The S-T segment will be displaced (Fig. 3B) not by the original current of injury (designated I) but rather by an equivalent double layer oriented in the reverse way, called –I.[20] If the exploring electrode is nearer the injured than the uninjured side of the cell as shown in the figure, the displacement of the S-T segment will be upward or positive and toward the original baseline before the current of injury displaced it.

Theoretically, and clinical evidence of several kinds supports it, a degree of injury may exist in which the resting cell shows no abnormality, but depolarization of it may not be complete (Fig. 3C). The wave of excitation may be regarded as being blocked at the injured site and acting there as a standing wave or interface with its positive surface toward the injured region. As with the current of injury, the S-T segment will be elevated when the electrode is on the positive side of it, but in this instance a new current, D, dependent on the existence of a demarcation potential,* is flowing during systole rather than abolished. It can be represented as a change of the baseline to a new positive level if the exploring electrode bears the same relation to the cell as in the previous example. To be noted is that the equivalent electrical effect is the same as if a current of injury were assumed to exist during diastole (Fig. 3B and C). It is this mechanism which is suspected of being responsible for the displacement of the S-T segment which may occur spontaneously or following effort or induced hypoxemia in patients with anginal syndrome. It is also believed to be the mechanism involved when pressure is made on the endocardium with the cardiac catheter.

A fourth type of injury is theoretically possible (Fig. 3D). It is a combination of the second and third types. The equivalent effect is similar to but larger than the equivalent effect of either of the previous two types individually. In clinical infarction it is very probable that this combination is involved.

* The term, demarcation potential, is used by the neurophysiologist[21] to describe the difference in electrical energy which results from differences in electrical properties of adjacent segments of nerve, and in this sense includes injury potentials. For the purpose of this presentation, demarcation potentials and injury potentials, and the currents which result from them, are regarded as differing from each other in the manner depicted in Figure 3 B, C, and D.

The fifth type of injury has been seen during the use of the electrode catheter. It consists of a large long negative potential occurring in diastole, and at a time when a U wave, if present, would appear. It is suggested that this phenomenon is caused by hyperpolarization such as seen in some of the experiments on the cell. The probable electrical situation is shown schematically in Figure 3E.

A sixth type of injury which is difficult to illustrate diagrammatically is of considerable clinical significance and has been ascribed to ischemia.[20] It is a degree of injury which does not result in subnormal repolarization or depolarization but rather in a delay in the rate of repolarization in some part of the cell (or in some part of the heart). This difference in the duration rather than magnitude of the excited state results in an abnormal final deflection or T wave. This "gradient" in the rate of recovery is accurately defined, as noted above, by the vectorial sum of the mean vectors representing depolarization and repolarization. In the clinical electrocardiogram it is determined from the area of QRS and T. In Einthoven's triangle (frontal plate of the body) its direction is usually such as to make an angle with the horizontal (angle α) of 0° to 90° and its mean length is approximately 50 microvolt seconds (μvs).

Clinical Considerations of Myocardial Injury

Because of the limited definition of injury made earlier, no discussion will be included of such electrocardiographic manifestations of injury as atrial and ventricular dysrhythmias, and atrioventricular and intraventricular block.

From what has been presented thus far it must be clear that the knowledge now possessed regarding the individual cell is applicable with only slight modification to an aggregate of cells or the heart as a whole.

In the atria: The atria differ from the ventricles in that no specialized conduction system is believed to exist for them. This makes the problem easier in that the atrial muscle may be regarded as a large syncytium over which excitation and recovery pass in a radial manner from the pacemaker, the sino-atrial node.

It has been shown experimentally that the accession and regression processes behave as though they were dipoles or double electric layers proceeding across the muscle. If the wave of accession behaves as a dipole with the positive pole in the direction of movement, and the wave

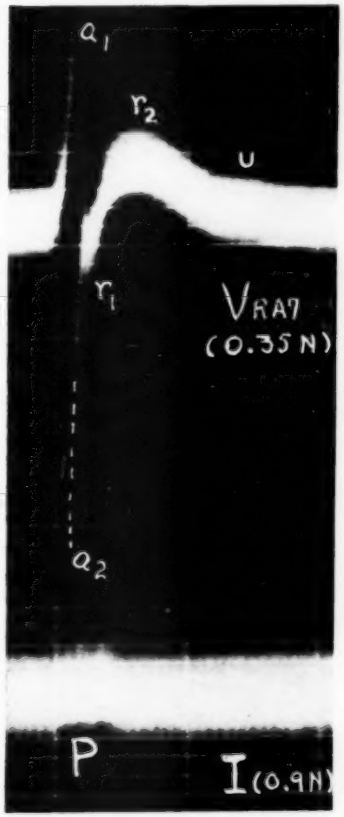

Figure 4—An enlarged electrogram (V_{RA_1}, upper record) made from the interior of the right atrium simultaneous with lead I (I, lower record) in a patient with complete atrioventricular block. The lower record is somewhat distorted by "hum" but the relatively simple, notched P wave (P) can be seen. Its actual complex structure at its source can be seen in the upper record in which five different deflections are recognizable. The waves a_1 and a_2 are the accession deflections (MacLeod); the latter is barely visible. The waves r_1 and r_2 are the regression deflections which are of reverse direction, longer duration, and lower amplitude than a_1 and a_2. The slow terminal positive wave labeled U is of unknown origin. The rapid change from a_1 to a_2 which was so rapid it was not photographed, is the "intrinsic deflection" which delineates the period of increasing activity of the cell (depolarization or rapid disappearance of the membrane potential, Fig. 1 and Fig. 2, AB). The slower change from r_1 to r_2 delineates the period of decreasing activity of the cell (repolarization or slow restoration of the membrane potential, Fig. 1 and Fig. 2, CD).

Time lines occur every 0.2 sec. The figures, 0.35N and 0.9N, indicate the sensitivity of the respective strings when the records were made (Kossmann, Med. Cl. N. A. 34:833, 1950).

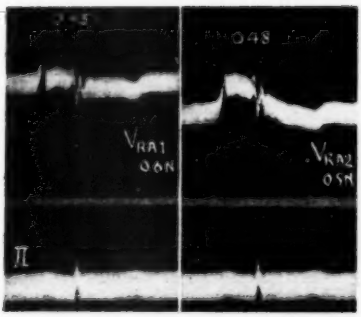

Figure 5—Right atrial electrograms (V_{RA_1} and V_{RA_2}) recorded from adjacent points in the right atrium of a normal man simultaneously with lead II (II). The second differs from the first by the presence of a contact or demarcation potential manifested by an elevation of the S-T segment which extends through and displaces the initial ventricular deflections, QRS, but has no effect on standard lead II.

The figures .045 and .048 indicate the time in seconds between the beginning of the P wave in lead II and the beginning of the intrinsic deflection in the electrograms. The figures 0.6N and 0.5N indicate the fraction of normal sensitivity of the string galvanometer used when the records were made. Time lines, 0.2 sec.

of regression behaves as a dipole with the negative pole in the direction of movement, then a quadriphasic curve would be expected, as noted earlier, when an electrode is placed directly on or close to the endocardial or epicardial surface of the atrium. In order to free the curve of the electrical effects of the normally sequential ventricular deflections, efforts to demonstrate this should be made preferably in a heart displaying a long atrioventricular conduction time or even complete atrioventricular block. A record from the atrium of a patient with the latter defect in conduction was made (Fig. 4). The rapid initial accession deflections are easily recognized as being diphasic, with the first phase (a_1) positive and the second (a_2) negative. The regression deflections are smaller but longer with the first (r_1) negative and the second (r_2) positive. The period of possession (a_2 to r_1) is very brief.

The patient had arteriosclerotic and rheumatic heart disease and at necropsy the right atrium was abnormally large. The atrial electrogram cannot, therefore, be accepted as a normal but it does demonstrate the basic electrophysiology involved which agrees, with the exception of the U wave, with the experimental findings in the frog's atrium made by Macleod.[13] The U wave, positive in this instance, may be on the basis of inductance in the non-excitable endocardium brought about by the trailing edge of the wave of regression.

When the electrode makes pressure on the endocardial surface of the atrium, the curve becomes distorted in a characteristic way (Figs. 5 & 6). The junction between the initial and final atrial deflections (S-T_p Junction or Jp) invariably becomes elevated, and the initial deflections (QRSp) may be modified usually by a reduction in the size or obliteration of the S_p wave. The duration of recovery (J-T_p interval) appears to be lengthened. All of the phenomena disappear promptly when the electrode either spontaneously or by design no longer makes pressure on the endocardium. The modifications of the initial and final atrial deflections may be encountered in either atrium. They have been observed when the catheter was in the coronary sinus or one of its venous tributaries, and have been seen intermittently with atrial flutter (Fig. 7).

The phenomenon is attributed to a block of the wave of depolarization at the electrode so that the latter is electrically positive during systole. The situation is thought to be comparable to what is shown diagrammatically in Figure 3C, with the probable addition (not shown) of a slower rate of repolarization. The electromotive force generated

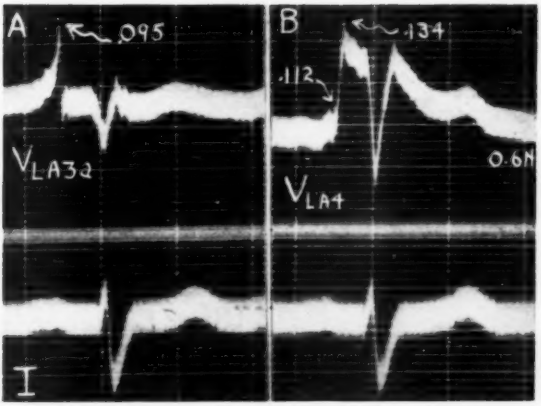

Figure 6—Left atrial electrograms (V_{LA_3a} and V_{LA_4}) recorded from adjacent points in the left atrium of a man with an atrial septal defect simultaneously with lead I. Record B shows the distortion caused by contact of the electrode with the endocardium. Numbers and time lines are as in Fig. 5.

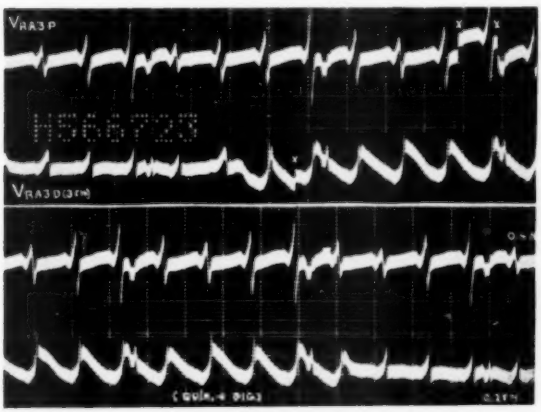

Figure 7—Atrial flutter with intermittent demarcation potential. The record is a continuous one. A double electrode catheter was used. Each electrode was 1 mm in length, and the distal ends of the two were separated by a distance of 3 cm. The electrogram from the proximal electrode (V_{RA_3P}) shows no distortion of the S-T segment, although there is some variation in the initial atrial deflections probably caused by movement of the electrode. The electrogram from the distal electrode (V_{RA_3D}) shows a spontaneous occurrence of displacement of this segment toward the end of the upper strip and a spontaneous disappearance at the end of the lower. The x marks points at which a standardizing current was passed through the string. Ventricular deflections may be recognized as occurring in a ratio of 1:4 to the P waves. The patient was receiving quinidine and digitalis. Time lines, 0.2 sec.

under such conditions is sharply localized to the exploring electrode itself and does not affect the S-T_P segment of a simultaneous standard lead or precordial lead made over the intracardiac electrode. It is doubtful that a current of injury exists during diastole (Fig. 3B) because the force under consideration, which may be regarded as arising from a demarcation potential or pressure potential, promptly disappears when pressure on the endocardium is released. This is in contrast to the injury current which is ascribed to a more serious degree of impairment of electrical function due to actual depolarization of part of the cell or some of the aggregate of cells. It disappears gradually over a period of time as the injured cells either undergo necrosis or recover.

There appears to be no spontaneous clinical counterpart of the atrial demarcation current as observed with the catheter. However, injury potentials, theoretically at least, can exist with infarction of the atrium or involvement of it by inflammatory or neoplastic disease. Whether the P-R segment, measured from the end of the P wave to the beginning of ventricular QRS, is elevated or depressed as a result of such injury potentials will depend on the orientation of the electrodes used in the surface lead with respect to the equivalent double electric layer resulting from the injury (Fig. 3B). It must be kept in mind, too, that the P-R segment will be displaced by such factors as digitalis and tachycardia by virtue of their effect on the regression process in the atria. Theoretically the P wave itself may be modified in form if destruction of atrial musculature is extensive.

The incidence of infarction in the atria is higher than most pathological data indicate. In the series studied by Cushman, Feil and their associates[22] there were 31 instances (17.0 per cent) of atrial infarction among 182 cases of myocardial infarction. The great majority (21 cases) were in the right auricular appendage and were accompanied by mural thrombosis as well. Although the majority displayed abnormalities of the atrial mechanism, only five displayed depression of the P-Q segment. Other reports of alterations both in P wave and P-Q segment have been made and one experimental study of the effects of alcohol induced necrosis[23] suggests that the P-Q segment may be elevated in lead I with left atrial injury, and elevated in leads II and III with right atrial injury, both accompanied as well by a change in amplitude and form of the P wave. Clinical confirmation of this finding has not been forthcoming.

With neoplastic involvement of the atria[24] disturbances of rhythm

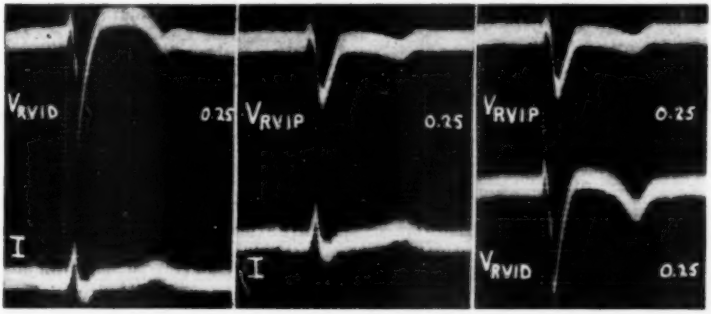

Figure 8—Endocardial potentials of the right ventricle in a patient with right bundle branch block. The double electrode catheter was used with electrodes 3 cm apart. The first record ($V_{BV,D}$) recorded from the distal electrode simultaneously with lead I (I) shows elevation of the S-T segment. The record from the proximal electrode ($V_{BV,P}$) shows no distortion of this segment. When the recording was made simultaneously from the two intracardiac electrodes (third record), some but not all of the S-T elevation had spontaneously subsided. Time lines, 0.2 sec.

seem to be more common than abnormalities of the initial or final atrial deflections.

In summary, it may be stated that experimental and clinical studies of the electrical behavior of the atrial myocardium have been most valuable in elaborating and crystallizing the present state of knowledge concerning the normal and abnormal electrophysiology of the heart. The practical use of this information as applied to the atria has been limited because of the relative infrequence of dynamically important disease of these chambers, and the dominance of rhythmic disturbances rather than electrocardiographic abnormalities resulting from a change in the extent, rate, or course of depolarization or repolarization.

In the ventricles: As in the right atrium, demarcation potentials may be encountered during catheterization of the right ventricle[25] or of the left ventricle.[26, 27] These are accompanied by a variety of modifications of the preceding deflections of depolarization. Sometimes the initial positive deflection and deep, notched negative deflection characteristic of a right ventricular lead are not modified at all or only slightly by the demarcation potential (Fig. 8); in other instances the S wave is almost completely eliminated, making the curve appear, in a sense, monophasic (Fig. 9). It is suspected that obliteration of the QRS deflection is largely an algebraic effect on the electrode of two oppositely oriented double

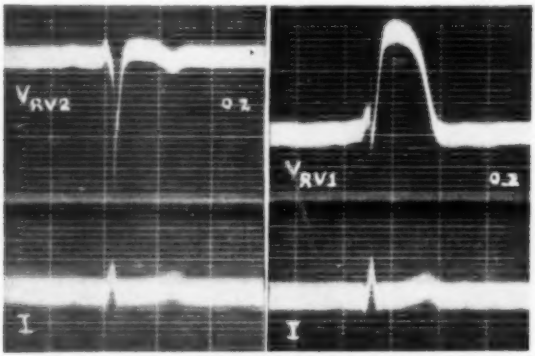

Figure 9—Leads from adjacent points in the right ventricle of a normal man showing the "monophasic" distortion which occurs (V_{RV_1}) when the electrode makes pressure on the endocardium. The similarity of the earliest parts of QRS in both records is to be noted. The simultaneous lead is I, recorded at somewhat less than normal sensitivity with V_{RV_2}. Time lines, 0.2 sec. (Kossmann et al, *Circulation* 2:10, 1950).

electric layers. The contact potentials are not reflected in surface leads (Fig. 10).

As in the atria, no exact clinical counterpart of this catheter pressure potential occurs unless it be the rare example of a tumor[28] or foreign body pressing on the heart, or the abnormal mechanics at the margins of a ventricular aneurysm.[29] A degree of excitation block is regarded as accompanying all injury currents by some.[30] It is likely that the temporary S-T displacements seen in anginal syndrome are on this basis, the block being induced by a relative vascular insufficiency of short duration.

On the other hand, injury phenomena of longer duration are common in the ventricles and depending on the degree, may modify the QRS deflections, the S-T segment, the T wave, or combinations of these.

The changes which occur in QRS, other than those caused by intraventricular block, are due to the loss of muscle elements which ordinarily contribute to the total of the deflections resulting from depolarization of the ventricular muscle. The best known change, alluded to earlier, is the subendocardial or transmural destruction of the wall of a chamber, usually the left ventricle, resulting in a surface lead becoming a semidirect lead from the cavity of that chamber.

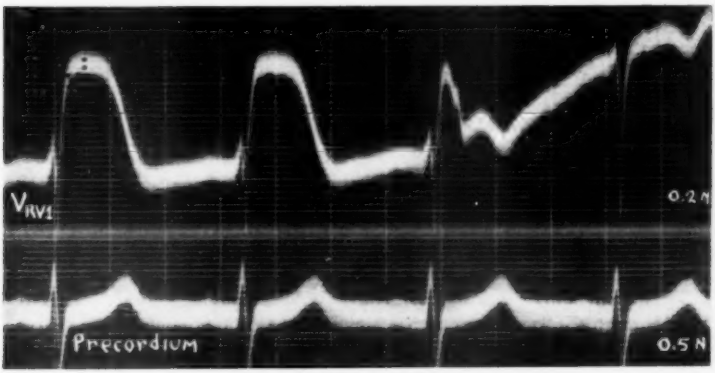

Figure 10—Contact potential shown in a lead (V_{RV_1}) from the cavity of the right ventricle of a normal man which disappears as the electrode is slowly withdrawn. The distortion of the baseline at the end of the trace is presumed to be due to breaking of the endocardial contact. The last complex is probably a record of the true cavity potential before distortion. The simultaneous lead made with an electrode placed on the chest wall directly over the intracardiac electrode shows no change as the demarcation potential is made to disappear. Time lines, 0.2 sec.

One of the earliest changes in the electrocardiogram which occurs with coronary closure is rarely seen in clinical curves but has been produced in animals.[31] When a coronary artery is tied off in a dog the initial change is in the T wave, not in the S-T segment. This is ascribed to ischemia with a delay in the velocity of the repolarization process in the involved muscle. As the ischemia becomes more severe, necrosis results, and there is then superimposed the effects of an injury current which tend to displace the S-T segment in a direction opposite to the abnormal T wave. Once the injury current subsides, as the cells responsible for it either die or recover, the S-T segment returns to the baseline, and the delayed recovery in the "ischemic" muscle adjacent to the dead zone again results in abnormal T waves of a type which are well known clinically.

An observation of some interest and without a satisfactory explanation is the occurrence of elevation of the S-T junction and segment in precordial leads when there is infarction in the anterior part of the heart, and depression of this junction and segment when there is infarction in the posterior part of the heart. The spatial axis of injury, E_J, points upward, forward, and to the left in the anteroseptal infarct (Fig. 11B);

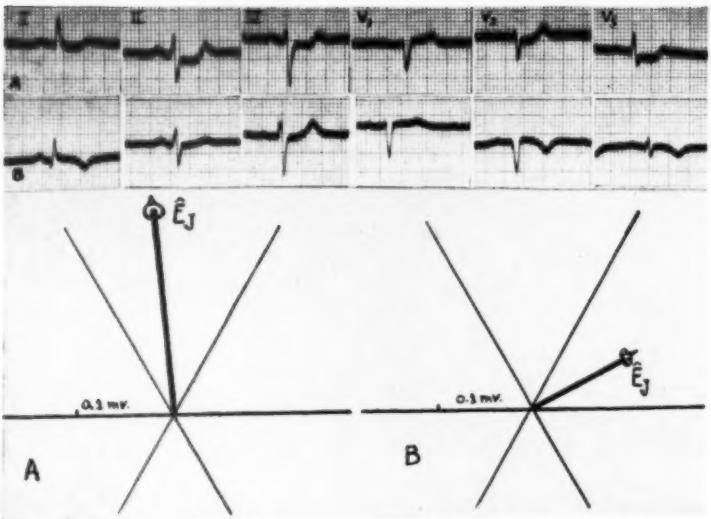

Figure 11—Changing spatial axis of injury, E_J, in a male patient with recent myocardial infarction. Record A was made approximately two hours after, and record B 40 hours after symptoms began. The initial spatial axis of injury is directed upward, backward, and to the right as expected with a subendocardial lesion. The final axis of injury is upward, forward, and to the left as usually seen with infarction in the anterior part of the heart. The change is ascribed to the lesion becoming transmural, which is supported by the changes in QRS which have occurred between the two curves. Time lines, 0.04 sec. (see Fig. 13 A and B).

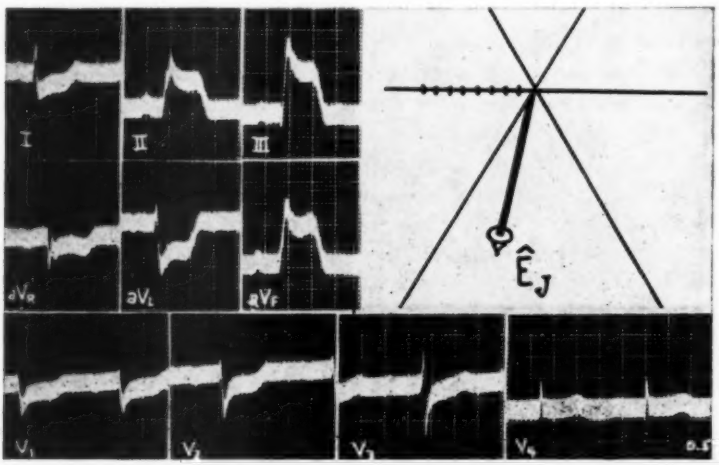

Figure 12—Unusual displacement of the S-T segment in an elderly female after myocardial infarction. The spatial axis of injury, E_J, has a direction downward, backward, and to the right as expected in posteroseptal infarction. Changes in QRS are not yet fully developed.

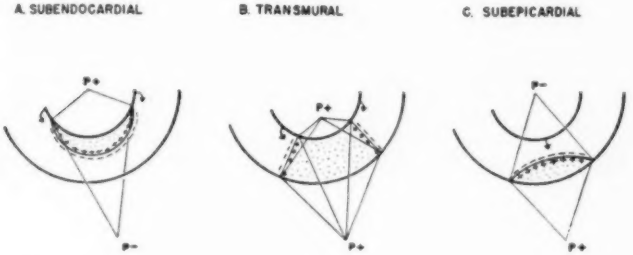

Figure 13—Diagram of the electrical effects of a subendocardial, transmural, and subepicardial lesion. The semicircular diagrams represent a portion of the ventricular wall. The stippled areas are dead, the clear areas healthy muscle, and between the two is assumed to be an injured area where excitation is blocked as it approaches it from the endocardial surface (arrows). The variable electrical effect on points, P, inside and outside of the chamber, are on the basis of the relationship, $V = \phi\omega$ (see Fig. 2).

downward, backward, and to the right in the posteroseptal infarct (Fig. 12). On theoretical grounds (Fig. 13A) the reverse should be the case because infarction in the heart is usually more extensive on the endocardial than on the epicardial surface, and a good many do not extend to the epicardial surface at all. Under such circumstances the exploring electrode, in the case of an anterior subendocardial infarct, should be on the normal side of a junction between normal and injured tissue. During electrical systole the electrode would then be negative with respect to surrounding medium as a result of the vector, E_J (or $-I$), being directed away from the normal muscle (Fig. 13A).

Several explanations have been given. Bayley[20] pointed out that with transmural infarction a subendocardial layer of healthy muscle is preserved, under which circumstances the normal–injured junction would have a reverse orientation of that expected on the basis of the distribution of the coronary blood supply. In experiments on turtles and dogs, Pruitt and Valencia[32] demonstrated that preservation of a subendocardial layer is not essential to the production of an elevated S-T junction in direct or semidirect epicardial leads from an area of myocardial destruction. In their experiments, positive displacement was also observed when an electrode was placed on the cavity side of a transmural lesion. They attributed upward displacement of the S-T segment on both aspects of the lesion to boundaries developed between injured and uninjured

muscle at the margins of their experimentally produced lesions (Fig. 13B).

Rarely in the course of myocardial infarction in the anterior part of the heart a transition is seen in serial records between the theoretically expected downward displacement of the S-T segment in precordial leads and the more usually encountered upward (positive) displacement of this segment. This is demonstrated in Figure 11. The initial record, A, was made approximately two hours after the onset of the clinical syndrome of coronary occlusion with myocardial infarction in a middle aged man. In it the S-T junction and segments are depressed in the standard and precordial leads. The spatial axis of injury[29, 33] or instantaneous vector for the S-T junction, E_J, is directed upward, to the right, and backward. This is the direction expected with a subendocardial lesion (Fig. 13A) and is the usual direction taken by this vector when temporary angina occurs spontaneously, is produced by hypoxia or exercise,[34, 35] or occurs with tachycardia, hemorrhage or peripheral circulatory failure in the syndrome called coronary insufficiency.[36-38] Approximately 48 hours later, however, (Fig. 11B) the S-T junctions have the more usual reciprocal displacement in the standard leads I and III with elevation in lead I and in the left sided precordial leads. The vector has changed to an anterior, upward and leftward direction. The change is ascribed to early involvement of subendocardial muscle only, similar to what is shown diagrammatically in Figure 13A, and to later transmural involvement, as shown diagrammatically in Figure 13B.

One of the problems of clinical electrocardiography has been the difficulty of telling whether myocardial injury is present when there is a complete defect in conduction in the left bundle branch. The problem is best illustrated by an example (Fig. 14) of a patient who had a recent infarct of the heart, and who displayed intermittent left bundle branch block, as well as atrioventricular block, over a period of several days. The figure shows the forms of the QRS and T waves with and without block. Lead V_2 shows how the broad, deep T wave caused by delayed subepicardial repolarization is completely obscured and replaced by an upright T when block of the bundle develops. A similar phenomenon, in lesser degree, is displayed by the other leads.

The case relates to the matter of the ventricular gradient,[14, 39] already touched upon in the discussion of the electrical behavior of the cell. Stated as simply as possible, the T wave may be modified by two known variables. First, it may be modified by a change in the mean direction

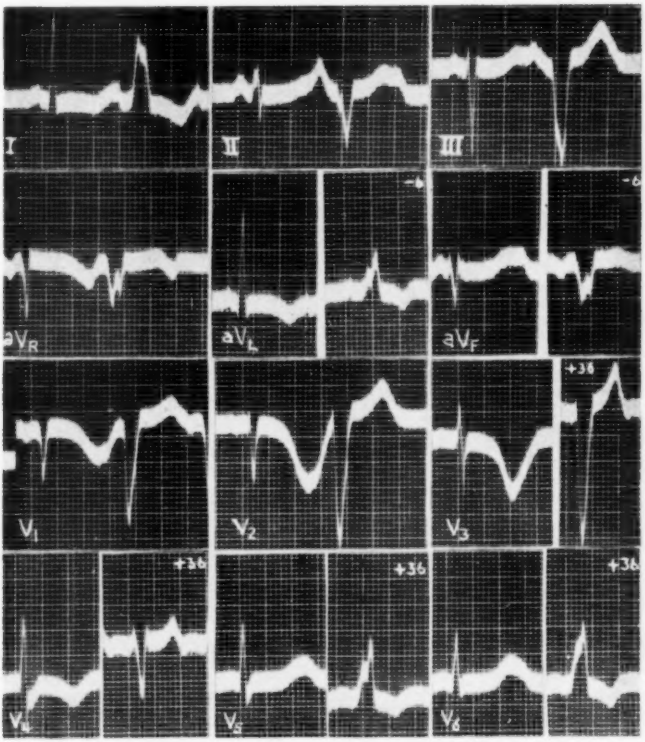

Figure 14—Myocardial infarction with intermittent left bundle branch block and complete and incomplete atrioventricular block. In the standard leads, and leads aVR, V_1 and V_2, adjacent complexes show the presence and absence of the bundle branch block. In the other leads the two types were recorded at different times. The figures —6 and +36 mean that the record on which they appear was recorded 6 hours earlier or 36 hours later than the other in the same lead.

In adjacent complexes, supraventricular and aberrant, on the same strip, the area of QRST is approximately the same.

The figure illustrates the obscuration by left bundle branch block of the primary abnormalities of the T wave.

of excitation, or QRS. Under such circumstances it follows that the mean direction of recovery must of necessity also be changed. This is illustrated by the considerable alteration in the T wave which occurs where there is intermittent bundle branch block without infarction. In this instance the ventricular gradient is exactly the same after as it was

before the block. Second, the T wave may be altered by any process, such as infarction or pericarditis, which delays regression locally. When both variables are operative, as in the case shown (Fig. 14), a calculation of the magnitude and direction of the gradient, which is a vectorial sum of the mean manifest potentials of QRS and of T, may indicate by its abnormality that there is local injury grossly obscured by the bundle branch block.

To return to the figure, it will be noted that the primary abnormality of the T wave is obscured whenever the area of the QRS deflections during block is large. This amounts to saying that the secondary change in T wave is greater than the primary change. Further, the effects of the infarct on QRS may be obscured by virtue of the fact that the mean direction of excitation of the septum, being from right to left in left bundle branch block, makes the left ventricular cavity positive. Semidirect leads from the cavity will then be, at least partially, positive rather than negative as when intraventricular and septal conduction are normal. This was not true in the present case because the infarct had caused little change in the supraventricular QRS.

Although a great deal of information is available on the ventricular gradient,[40-43] including its usual orientation in infarction and acute pericarditis,[33] nevertheless it has not been used clinically except in a gross manner for the reason that it cannot be measured too accurately or easily.[44] As soon as simpler instrumental means are available, it is probable that the measurement will be made routinely and have considerable practical value.

A curious type of record has been encountered several times during cardiac catheterization. It is characterized by a large negative potential occurring toward the end of the T wave and extending well into the ordinarily isoelectric T-P interval (Fig. 15). It has been observed to have a magnitude of as great as 8.0 mv, and its position in the ventricular electrocardiogram is about where the U wave would be expected. This negative potential may be on the basis of hyperpolarization (Figs. 1 and 3E) brought about in some way by the pressure of the catheter-electrode on the endocardium of the right ventricle. As can be seen in Figure 15, this potential is not reflected in a surface lead, varies in degree (lowest trace in figure), and disappears as soon as pressure of the electrode is released (end of top trace in figure). It is suspected that this type of injury may manifest itself clinically by modifications in the U wave which have heretofore been relatively neglected.

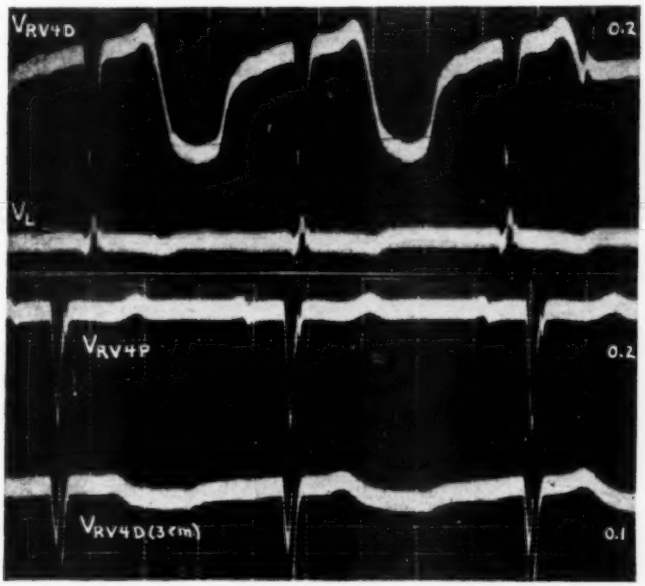

Figure 15—Intracardiac leads in a Negro male with unknown heart disease displaying a late, large, negative potential possibly caused by hyperpolarization (see Fig. 3E). The upper record ($V_{RV,D}$) from the right ventricle, made simultaneously with the potential of the left arm (V_L) shows a spontaneous disappearance of the potential at the end of the strip.

The lower records were made with a double electrode catheter in the right ventricle with the electrodes 3 cm apart. The proximal electrode recorded the probable true potential of the cavity ($V_{RV,P}$); the distal electrode recorded the negative after potential but in lesser degree than initially ($V_{RV,D}$). To be noted is the occurrence of this potential near the end of the T wave and its persistence for almost 0.3 sec. into the T-P interval. Time lines, 0.2 sec.; string sensitivity is normal unless otherwise indicated.

In summary, it may be concluded that experimental and clinical studies of the electrical behavior of injured ventricular muscle have shown a high degree of correlation, one with the other. What minor discrepancies still exist, particularly between what is observed electrocardiographically and what is found anatomically, may be ascribed to the considerable disturbance in electrical behavior which occurs in the course of injury well in advance of anatomical changes which can be detected by present methods.

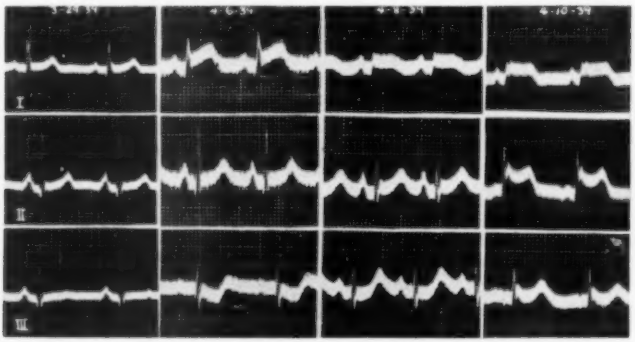

Fig. 16—Standard leads before (3-29-39) myocardial infarction, after (4-6-39, 4-8-39) myocardial infarction, and after (4-10-39) development of fibrinopurulent streptococcus pericarditis. To be noted is the discordant displacement of the S-T segments in the second two curves and the concordant displacement of these segments in the last.

Clinical Considerations of Pericardial Injury

It is generally agreed that the pericardium is a passive conductor. Electrocardiographic abnormalities which occur with disease of or trauma to this membrane are ascribed to involvement of the subepicardial myocardium. An exception is the case of the massive pericardial effusion which theoretically causes some diminution in the size of all electrocardiographic deflections by virtue of its short-circuiting effect.

The changes which occur in the clinical electrocardiogram are well known.[45] During the first week of an acute pericarditis, with the exception of uremic pericarditis, the S-T segment is characteristically elevated in leads I, II, V_L, and left sided precordial leads, and depressed in leads V_R and V_1. Usually there is little or no deviation of the segment in lead V_F. During the inscription of the T wave the potential of the right arm and of the right sternal edge is negative, of the left arm and left leg variable and of the precordial leads, other than V_1, positive and possibly notched. The spatial axis of injury is downward, forward and to the left (Fig. 11C).

In a period of a few days up to several weeks there is gradual disappearance of the abnormal S-T segments, and reverse modifications in the T wave occur. In leads V_R and V_1 this deflection becomes positive, and in the standard leads and the leads from the left side of the precordium

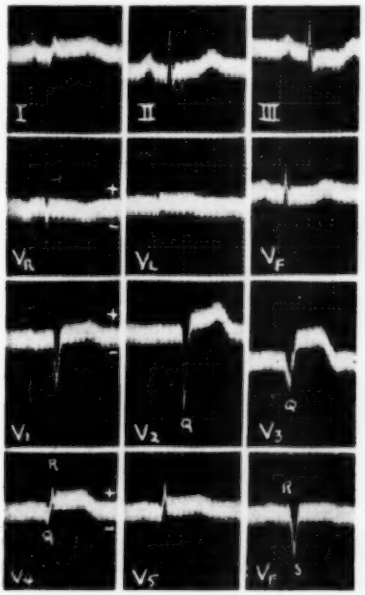

Fig. 17—Standard leads (I, II, III), extremity potentials (V_R, V_L, V_F), and precordial potentials (V_1 to V_6, and V_E, tip of ensiform) in same patient as in Fig. 16 recorded on 4-7-39. The changes are typical of transmural anteroseptal infarction with probable subendocardial involvement at the apex. Chest leads were recorded at 0.5N sensitivity of the string. Time lines, 0.04 sec.

it becomes negative or less positive. In the leads from the left arm and the left leg the modifications are variable.

The characteristic concordant elevation of the S-T segments and subsequent concordant depression of the T waves in the standard leads are ascribed to involvement of the subepicardial myocardium around the apex dominantly on the anterior wall (Fig. 11C). It hardly need be pointed out that pericarditis does not occur exclusively in this area, that a similar electrocardiographic picture will be obtained if the lesion is diffuse, and that other abnormalities observed will depend on the orientation of the injured and ischemic myocardium to the surface electrodes. Further, pericarditis may exist without any electrocardiographic abnormalities.

A problem of considerable practical interest is the differentiation of the electrocardiographic effects of pericarditis from those of myocardial infarction, especially since approximately 15 per cent of myocardial infarcts are complicated by a diffuse pericarditis.[46] When the electrocardiograms are characteristic, the differential diagnosis is fairly easy, although exceptions occur particularly if the infarction is diffuse or if there are multiple infarcts. If in the course of myocardial infarction known to be elsewhere than at the apex a concordant displacement of the S-T segment occurs, almost certainly pericarditis is complicating the picture. The example (Figs. 16 and 17) shows a control electrocardiogram (3-29-39) and two sets of standard leads (4-6-39 and 4-8-39) made after the clinical occurrence of myocardial infarction probably on 4-3-39. The precordial and extremity leads were made on 4-7-39 (Fig. 17). The three latter records leave little doubt about the recent occurrence of myocardial necrosis involving most probably the anterior wall of the left ventricle, and the adjacent anterior interventricular septum but not the apex (see leads V_4 and V_5). On 4-10-39, however, the standard leads display a new concordant deviation of the S-T segments, ascribed to a subepicardial myocarditis oriented in such a way as to yield an axis of injury directed downward and to the left. No pericardial friction rub was heard. Nevertheless this new finding suggested diffuse pericarditis, and the axis of injury indicated that the original infarction was not apical, or at least not transmural at the apex, for under such circumstances the subepicardial muscle would be dead, and the complicating pericarditis could not then have caused the direction that the new axis of injury took.

At necropsy there was a fresh occlusion of the anterior descending branch of the left coronary artery. The infarct was dominantly on the anterior wall of the left ventricle but did extend to the apex. In the latter region, however, the infarct was subendocardial only, and covered by a mural thrombus. There was, in addition, a diffuse fibrinopurulent pericarditis which yielded on culture a hemolytic streptococcus. The probable portal of entry of this organism was in an area of freshly consolidated lung. All subserous layers of the ventricular myocardium which were examined displayed a heavy infiltration with polymorphonuclear leukocytes.

Even with infarction in other areas of the heart, the occurrence of concordant elevation of the S-T segments in the standard leads should excite suspicion of a complicating diffuse pericarditis. Although the diag-

nosis formerly was only of academic interest, in this era of potent antibiotics the recognition and energetic treatment of the purulent types may be life saving.

From the discussion, it is apparent that an apical infarct can simulate, exaggerate, or nullify the electrocardiographic effects of a diffuse pericarditis depending on its intramural location.[20] It also must be clear that the local pericarditis which occurs over a transmural infarct probably has no electrical effects because the muscle under it is necrotic and electrically inert.

One possible manifestation of injury which has been observed in this laboratory to occur with unusual frequency in acute pericarditis is electrical alternans involving both QRS and T.

Summary

The several varieties of "injury" of the myocardium and pericardium which may be reflected in the electrocardiogram have been reviewed. An attempt has been made to demonstrate how an understanding of the membrane theory coupled with a knowledge of the behavior of electrical currents in volume conductors make it possible to draw a conclusion in physiological terms and with a great deal of precision regarding the nature of the clinical disturbance which may be present. It is suggested that the era of describing, classifying, and cataloguing the nature and behavior of the action potential of the heart in a conducting medium is drawing to an end, and it is visualized that the future holds considerable promise for the exact correlation of the electrical with other functions of the myocardial cell.

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[*REFERENCES ON NEXT PAGE*]

REFERENCES

1. Lewis T. and Gilder, M. D. D. The human electrocardiogram; a preliminary investigation of young male adults to form a basis for pathological study, *Philos. Trans. Roy Soc.* London, ser. B *202*:351-76, 1913.
2. Wilson, F. N., Macleod, A. G. and Barker, P. S. *The distribution of the currents of action and of injury displayed by heart muscle and other excitable tissues.* Ann Arbor, University of Michigan Press, 1933.
3. Bernstein, J. *Elektrobiologie.* Braunschweig, Friedr. Vieweg & Sohn, 1912.
4. Curtis, H. J. and Cole, K. S. Membrane resting and action potentials from the squid giant axon, *J. cell. comp. Physiol. 19*:135-34, 1942.
5. Hodgkin, A. L. and Huxley, A. F. Resting and action potentials in single nerve fibers, *J. Physiol. 104*:176-95, 1945.
6. Graham, J. and Gerard, R. W. Membrane potentials and excitation of impaled single muscle fibers, *J. cell. comp. Physiol. 28*:99-117, 1946.
7. Nastuk, W. L. and Hodgkin, A. L. The electrical activity of single muscle fibers, *J. cell. comp. Physiol. 35*:39-73, 1950.
8. Woodbury, L. A. Hecht, H. H. and Christoferson, A. R. Membrane resting and action potentials of single cardiac muscle fibers of the frog ventricle, *Amer. J. Physiol. 164*:307-28, 1951.
9. Woodbury, L. A., Woodbury, J. W. and Hecht, H. H. Membrane resting and action potentials of single cardiac muscle fibers, *Circulation 1*:264-66, 1950.
10. Cole, K. S. and Curtis, H. J. Electric impedance of nitella during activity, *J. gen. Physiol. 22*:37-64, 1938-1939.
11. Cole, K. S. and Curtis, H. J. Electric impedance of the squid giant axon during activity, *J. gen. Physiol. 22*:649-70, 1938-1939.
12. Kossmann, C. E. General crymotherapy: a symposium; cardiovascular aspects, *Bull. N. Y. Acad. Med. 16*:317-20, 1940.
13. Macleod, A. G. The electrogram of cardiac muscle; an analysis which explains the regression or T deflection; and the lengths of the stages of activity, *Amer. Heart J. 15*:165-86; and 402-13, 1938.
14. Wilson, F. N., Macleod, A. G., Barker, P. S. and Johnston, F. D. The determination and the significance of the areas of the ventricular deflections of the electrocardiogram, *Amer. Heart J. 10*:46-61, 1934.
15. Kossmann, C. E., Berger, A. R., Brumlik, J., and Briller, S. A. An analysis of causes of right axis deviation based partly on endocardial potentials of the hypertrophied right ventricle, *Amer. Heart J. 35*:309-35, 1948.
16. Wilson, F. N., Macleod, A. G., and Barker, P. S. The interpretation of the initial deflections of the ventricular complex of the electrocardiogram, *Amer. Heart J. 6*:637-64, 1931.
17. Kossmann, C. E. The interpretation of unipolar precordial electrocardiograms, *Med. Clin. N. Amer. 34*:833-55, May 1950.
18. Wilson, F. N., Johnston, F. D. and Hill, I. G. W. The form of the electrocardiogram in experimental myocardial infarction. Additional observations on the later effects produced by ligation of the anterior descending branch of the left coronary artery, *Amer. Heart J. 10*:1025-41, 1935.
19. Kossmann, C. E. Unipolar electrocardiography, including intracardiac leads, in the diagnosis of myocardial disease, *Bull. N. Y. Acad. Med. 26*:20-48, 1950.
20. Bayley, R. H. An interpretation of the injury and ischemic effects of myocardial infarction in accordance with laws which determine the flow of electric currents in homogeneous volume conductors, and in accordance with relevant pathologic changes, *Amer. Heart J. 24*:514-28, 1942.
21. DeNó, R. L. Correlation of nerve activity with polarization phenomena, *Harvey Lect. 42*:43-105, 1946-1947.
22. Cushing, E. H., Feil, H. S., Stanton, E. J., and Wartman, W. B. Infarction of the cardiac auricles (atria): clinical, pathological, and experimental studies, *Brit. Heart J. 4*:17-34, 1942.
23. Sanders, A. Experimental localized auricular necrosis; an electrocardiographic study, *Amer. J. med. Sci. 198*:690-94, 1939.
24. Mahaim, I. *Les tumeurs et les polypes du coeur.* Paris, Masson et Cie, 1945.

25. Kossmann, C. E., Berger, A. R., Rader, B., Brumlik, J., Briller, S. A. and Donnelly, J. H. Intracardiac and intravascular potentials resulting from electrical activity of the normal human heart, *Circulation 2*:10-30, 1950.
26. Sodi-Pallares, D., Estandía, A., Soberón, J., and Rodríguez, M. I. The left intraventricular potential of the human heart. I. Methods; II. Criteria for diagnosis of incomplete bundle branch block, *Amer. Heart J. 40*:650-54; 655-79, 1950.
27. Zimmerman, H. A. and Hellerstein, H. K. Cavity potentials of the human ventricles, *Circulation 3*:95-104, 1951.
28. Rosenbaum, F. F., Johnston, F. D. and Alzamora, V. V. Persistent displacement of the RS-T segment in a case of metastatic tumor of the heart, *Amer. Heart J. 27*:667-75, 1944.
29. Rosenberg, B. and Messinger, W. J. The electrocardiogram in ventricular aneurysm, *Amer. Heart J. 37*:267-77, 1949.
30. Bayley, R. H. On certain applications of modern electrocardiographic theory to the interpretation of electrocardiograms which indicate myocardial disease, *Amer. Heart J. 26*:769-831, 1943.
31. Bayley, R. H., LaDue, J. S. and York, D. J. Electrocardiographic changes (local ventricular ischemia and injury) produced in the dog by temporary occlusion of a coronary artery showing a new stage in the evolution of myocardial infarction, *Amer. Heart J. 27*:164-69, 1944.
32. Pruitt, R. and Valencia, F. The immediate electrocardiographic effects of circumscribed myocardial injuries: an experimental study, *Amer. Heart J. 35*:161-97, 1948.
33. Grant, R. P. and Estes, E. H. *Spatial vector electrocardiography.* Philadelphia, Blakiston Co., 1951.
34. Master, A. M. and Oppenheimer, E. T. A simple exercise tolerance test for circulatory efficiency with standard tables for normal individuals, *Amer J. med. Sci. 177*:223-43, 1929.
35. Levy, R. L., Williams, N. E., Bruenn, H. G. and Carr, H. A. The "anoxemia test" in the diagnosis of coronary insufficiency, *Amer. Heart J. 21*:634-56, 1941.
36. Büchner, F. *Die Koronarinsuffizienz.* Dresden, Theodor Steinkopff, 1939.
37. Friedberg, C. K. and Horn, H. Acute myocardial infarction not due to coronary artery occlusion, *J. Amer. med. Assoc. 112*:1675-79, 1939.
38. Master, A. M., Jaffe, H. L., Dack, S. and Grishman, A. Coronary occlusion, coronary insufficiency, and angina pectoris; a clinical and post-mortem study, *Amer. Heart J. 27*:803-16, 1944.
39. Wilson, F. N. The T deflection of the electrocardiogram, *Trans. Assoc. Amer. Phys. 46*:29-38, 1931.
40. Ashman, R., Byer, E. and Bayley, R. H. The normal human ventricular gradient. I. Factors which affect its direction and its relation to the mean QRS axis, *Amer. Heart J. 25*:16-35, 1943.
Ashman, R. and Byer, E. The normal human ventricular gradient. II. Factors which affect its manifest area and its relationship to the manifest area of the QRS complex, *Amer. Heart J. 25*:36-57, 1943.
41. Ashman, R., Gardberg, M. and Byer, E. The normal human ventricular gradient. III. The relation between the anatomic and electrical axes, *Amer. Heart J. 26*:473-94, 1943.
42. Ashman, R. The normal human ventricular gradient. IV. The relationship between the magnitudes, A_{QRS} and G, and deviations of the RS-T segment, *Amer. Heart J. 26*:495-510, 1943.
43. Ashman, R., Ferguson, F. P., Gremillion, A. L. and Byer, E. The normal human ventricular gradient. V. The relationship between A_{QRS} and G, and the potential variations of the body surface, *Amer. Heart J. 29*:697-703, 1945.
44. Johnston, F. D., McFee, R. and Bryant, J. M. An integrating circuit for measurement of the areas of the waves in the electrocardiogram, *Circulation 2*:5-9, 1950.
45. Kossmann, C. E. and Schneider, J. Potential variations of extremities and of precordium in pericarditis, *Proc. Soc. exper. Biol. Med. 37*:213-14, 1937.
46. Langendorf, R. The effect of diffuse pericarditis on the electrocardiographic pattern of recent myocardial infarction, *Amer. Heart J. 22*:86-104, 1941.

PATHOLOGIC PHYSIOLOGY OF MITRAL STENOSIS AND ITS SURGICAL IMPLICATIONS*

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THE development of a direct surgical attack on narrowed mitral valves raises many questions as to its efficacy. Wilcox and Grace[1] have objected on theoretical grounds, believing that surgery could offer little or no benefit in the majority of patients with mitral stenosis. Harken and his associates[2, 3] Glover, O'Neill, and Bailey,[4] Baker, Brock, and Campbell,[5] and Prip Buus[6] have recently reported clinical improvement of their patients following direct valvular surgery. The evaluation of operative results by clinical impression alone leaves much to be desired, however, because spontaneous changes frequently occur in the clinical course of these individuals. The advent of pulmonary vascular changes and of right ventricular failure, for example, may result in symptomatic improvement by relieving pulmonary congestion, yet marks the onward progression of the disease. Objective evaluation of mitral valve surgery is therefore not only desirable but necessary. Baker, Brock, and Campbell[5] have studied the cardiac output and pulmonary arterial pressure in four cases after mitral valvulotomy and we[7] have reported the post-operative changes in circulatory dynamics in six cases.

This study reviews the pathological physiology of mitral stenosis as it relates to mitral valve surgery and analyzes the pre-operative and early post-operative changes in circulatory dynamics in twelve patients with incapacitating mitral stenosis on whom mitral valvuloplasty was performed at the Peter Bent Brigham Hospital by Dr. Dwight E. Harken.

PATHOLOGICAL PHYSIOLOGY OF MITRAL STENOSIS

A diagram illustrating the pathological physiology of mitral stenosis is shown in Figure 1. A detailed description of the points that follow

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DIAGRAM OF PATHOLOGIC PHYSIOLOGY OF MITRAL STENOSIS

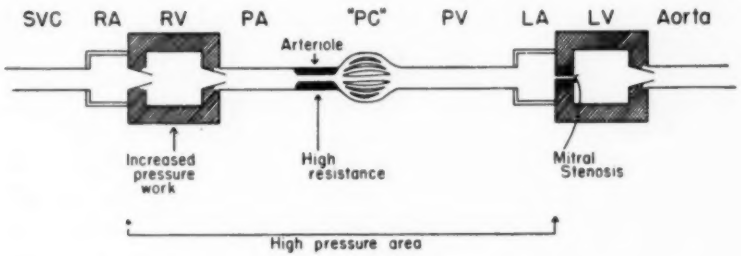

Fig. 1

have been published elsewhere.[8-12] It is to be emphasized at the outset that this discussion applies to mechanical mitral stenosis wherein there is no concomitant active rheumatic carditis.

The normal mitral valve has a cross-sectional area of 4 to 6 sq. cm. Methods have been developed by Gorlin and Gorlin[8] for accurately calculating the size of the orifice of the mitral valve during life in patients with mitral stenosis. In mitral stenosis, the orifice becomes narrowed and in the most advanced cases may be only 0.4 sq. cm. Narrowing of the mitral valve orifice produces an obstruction to the flow of blood at a critical point in the circulatory system, i.e., at a point just distal to the capillaries of the lung. Between these capillaries and the mitral valve there are no valves or other important buffering mechanisms. Indeed, in many ways the pulmonary capillaries, pulmonary veins, and left auricle can be thought of as a single vascular compartment with pressures in all parts not differing by more than a few mm. Hg. As the mitral valve orifice becomes narrower, it is obvious that if blood flow (cardiac output) is to be maintained at a normal level, pressure proximal to the mitral valve must increase. If pressure in the left auricle remains normal, blood flow must decrease. In mitral stenosis both occur, i.e., pressure in the left auricle and lung rises and cardiac output decreases. The pressure rise is predominant, however, and gives rise to the symptoms of dyspnea, orthopnea, paroxysmal nocturnal dyspnea, pulmonary edema, and hemoptysis, these being the prominent symptoms of mitral stenosis and the ultimate cause of disability. These symptoms are at-

tributable to a rise of pressure in the pulmonary capillaries to a level exceeding the osmotic pressure of plasma with the production of pulmonary edema. These two compensations – a rise of pressure proximal to the valve and a decrease in the amount of blood flowing through the valve – are the only two important compensations that take place during the time that the mitral valve is becoming narrower and narrower. Not until late in the course, when the valve becomes about 20 per cent of normal (about 1.0 sq. cm.) does the third compensation appear.

This compensation consists of narrowing of the arterioles and small arteries in the lung. Histologically there is intimal proliferation and medial hypertrophy.[13, 14] Physiologically, there is an increased resistance to blood flow through this segment of the lung which can easily be measured with the cardiac catheter.[9, 15] There is considerable variation in patients with mitral stenosis of the same severity in the extent of this vascular resistance in the lung. Some with tight mitral stenosis never develop important increases in resistance and these are the patients who have severe exertional dyspnea, orthopnea, hemoptysis, and attacks of acute pulmonary edema. These patients have hearts which are usually little if any enlarged and there is no venous distension, hepatomegaly, or other manifestations of right ventricular failure.[12] There are others who develop a moderate degree of pulmonary vascular resistance wherein there is a delicate balance between the resistances in the lung and at the mitral valve. These patients have few respiratory complaints because the right ventricle, due to the increased pulmonary resistance, cannot pump blood into the lung any faster than it can comfortably escape through the mitral valve. These two areas of increased resistance – the lung and the mitral valve – result in a low fixed cardiac output so that the predominant symptoms are fatigue, exhaustion, weakness, tiredness, ennui. At this point, the heart is enlarged, but the right ventricle is usually still competent. In some individuals, the pulmonary vascular resistance becomes excessive, i.e., 15 to 20 times the normal. The resistance to blood flow through the lung may become greater than that at the mitral valve. These individuals do not in our experience have episodes of pulmonary edema, but as in patients with severe cor pulmonale, there is excessive exertional dyspnea and orthopnea, the right ventricle becomes greatly enlarged and fails, with the appearance of venous distension, hepatomegaly, and edema.

The only clue to the mode of production of these pulmonary vascular lesions in mitral stenosis is that they make their appearance only late

in the course of mitral stenosis when the size of the mitral valve is about 1.0 sq. cm. or less, at which point even at rest pulmonary edema impends. It has been postulated[15] that this chronic threat of pulmonary edema in some unknown fashion leads to the appearance of the vascular changes. We have considered it to be a compensatory mechanism successfully preventing the right ventricle from sudden surges of output, thereby preventing the flooding of the pulmonary capillaries with blood.

The importance of this pulmonary vascular resistance cannot be over-estimated in modifying and influencing the clinical course of patients with mitral stenosis. Before its appearance, respiratory symptoms become increasingly prominent as the valve becomes narrower. It is not until the pulmonary resistance becomes five to ten times the normal level that the transverse diameter of the heart by x-ray becomes increased and respiratory symptoms decrease, and ten to fifteen times the normal that the right ventricle fails grossly.

Evaluation of Surgery

With these points in mind, it is obvious that relief of the stenosis itself may not necessarily result in clinical improvement of the patient unless the secondary changes in the lungs revert toward normal. As an amplification of an earlier report,[7] an attempt will be made to answer the following questions based on the findings shortly after operation in twelve patients on whom mitral valvuloplasty for severe, incapacitating mitral stenosis has been performed.

1. Can the mitral valve orifice really be widened?
2. Is mitral insufficiency necessarily produced?
3. Does the cardiac output increase?
4. Do pressures in the pulmonary circuit fall?
5. Does the increased pulmonary arteriolar resistance return to or towards normal?
6. Does right ventricular function, as indicated by its filling pressure, return to or towards normal?

Material

Twelve patients with mitral stenosis subjected to mitral valvuloplasty[16] in the Peter Bent Brigham Hospital were all incapacitated, many leading a bed and chair existence, and were graded as Class III or IV according to the New York Heart Association Classification. Studies were carried out a few days before operation and again between two

TABLE 1—CIRCULATORY DYNAMICS IN PATIENTS BEFORE AND AFTER MITRAL VALVULOPLASTY

Patient	Mitral Valve Stenotic Area cm.²		Cardiac Index l/min./sq.m.		Pulmonary "Capillary" Pressure mm. Hg.		Pulmonary Arteriolar Resistance dynes sec. cm.$^{-5}$		Right Ventricular Filling Pressure mm. Hg.		Mitral Regurgitation Present	
	Before	After	Before	After	Before	After	Before	After	Before	After	Before	After
M.McG.	0.4	0.7	1.8	1.9	25	17	770	889	4	4	0	0
W.F.	0.5	0.9	1.8	2.8	23	20	1139	332	8	6	0	0
R.W.	0.6	1.2	2.7	2.2	34	11	274	441	9	4	0	0
E.D.	0.6	1.5	2.4	1.9	36	21	411	600	12	4	0	++
J.G.	0.6	1.5	2.1	2.9	34	17	400	200	10	2	0	0
L.L.	0.7	1.3	2.5	2.6	27	24	632	554	5	13	0	0
T.C.	0.7	1.7	2.9	3.3	32	14	488	254	7	7	0	0
C.E.	0.8	1.7	2.2	2.8	18	11	292	173	5	3	0	0
B.A.	0.9	1.6	3.6	3.8	32	19	569	364	0	5	0	0
N.W.	1.0	1.6	3.2	3.6	33	19	204	280	2	4	0	0
E.L.	1.1	2.3	1.4	1.9	24	10	1480	523	5	4	++	++
A.D.	1.3	1.9	2.0	2.3	37	26	103	178	8	4	++	++

and six weeks after operation. Mitral insufficiency was detected qualitatively from the contour of the pulmonary "capillary" pulse tracing and estimated semi-quantitatively by means of hydraulic formulae.[17, 18]

METHODS

The methods have been described in detail elsewhere.[9] In general, they consisted of measuring cardiac output by the direct Fick principle and recording pressures with Sanborn electromanometers in the pulmonary "capillaries," pulmonary artery, right ventricle, right atrium, and brachial artery. From these pressure and flow measurements, calculations by the formulae described elsewhere[8] have been made of the size of the mitral valve orifice, and the pulmonary arteriolar and total pulmonary resistances. Estimates of the degree of mitral insufficiency, graded from one to four plus, have been based on the height of the v-wave in relation to the mean pulmonary "capillary" pressure.[17, 18]

Results

Pertinent data will be found in Table I and Figures 2 through 6.

1. *Size of the orifice of the mitral valve*: In each patient, the mitral orifice was significantly increased in size by operation (Figure 2). In eight, the size of the orifice post-operatively was considered to be satisfactory, i.e., greater than 1.5 sq. cm. If the size of the valve orifice were the only problem in mitral stenosis, these eight patients could be expected to return to almost normal activity. In R.W. and L.L., an adequate size of the valve orifice was obtained, i.e., 1.2 and 1.3 sq. cm. respectively. W.F. had an extremely elastic valve orifice which made finger fracture of the commissures difficult so that the resulting valve orifice measured post-operatively was only 0.9 sq. cm. The problem in her case was similar to that of trying to fracture a rubber band. Now that this problem is recognized, an appropriate surgical maneuver has been devised to overcome this difficulty. In M. McG., the anatomical nature of the stenosis made enlargement of the orifice technically almost impossible.

2. *Mitral insufficiency*: Nine patients had mitral stenosis without insufficiency before operation. None had mitral insufficiency post-operatively (Figure 2). Patients A.D. and E.L. had mitral stenosis and insufficiency before operation and, as nearly as could be judged, no definite change in their regurgitation either for better or for worse was produced by operation. In one patient, E.D., fracture of the valve commissure was carried forward unintentionally into the aortic leaflet so that some mitral regurgitation was produced. The dissection should have been carried to the annulus and no further or else into the minor leaflet. This must be regarded as a technical error incident to efforts at improving leaflet mobilization. Despite this one case, it is apparent that mitral valvuloplasty can relieve stenosis without producing regurgitation.

3. *Cardiac output*: Cardiac output was not significantly different two to three weeks post-operatively in the majority of patients (Figure 3). In W.F. and E.L. the cardiac output had increased appreciably, presumably due to the striking decrease of pulmonary arteriolar resistance. In J.G. and C.E., cardiac output rose significantly though not markedly. Baker, Brock and Campbell[5] found little change in cardiac output in four cases studied two to three months after surgery. The failure of cardiac output to increase shortly after operation may be due to the "disuse atrophy" of the left ventricle which occurs in mitral

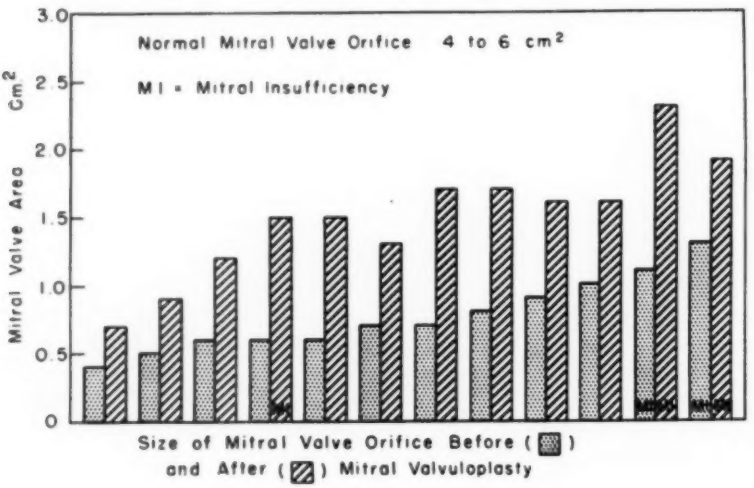
Normal Mitral Valve Orifice 4 to 6 cm²
MI = Mitral Insufficiency
Mitral Valve Area Cm²
3.0
2.5
2.0
1.5
1.0
0.5
0
Size of Mitral Valve Orifice Before ( ) and After ( ) Mitral Valvuloplasty

Fig. 2

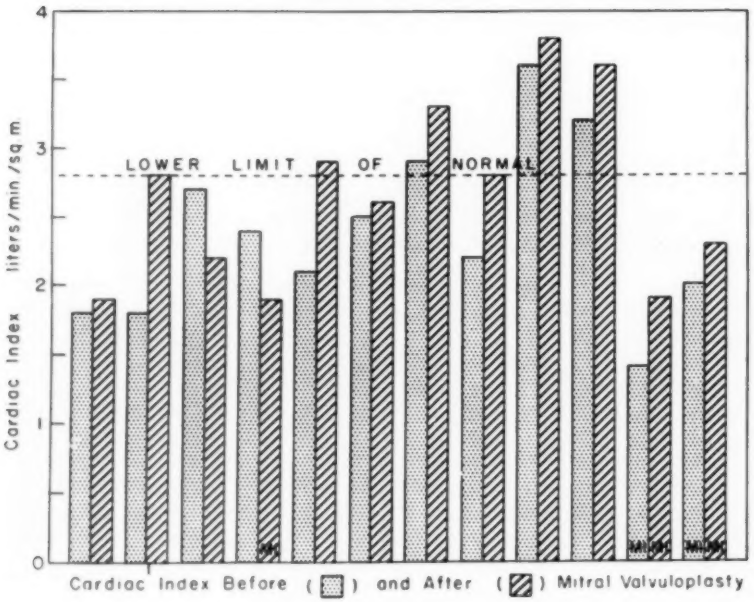
Cardiac Index liters/min/sq m
4
3
2
1
0
LOWER LIMIT OF NORMAL
Cardiac Index Before ( ) and After ( ) Mitral Valvuloplasty

Fig. 3

stenosis and to the increased resistance in the arterioles of the lung, which tends to keep the output of the right ventricle depressed in mitral stenosis as well as in cor pulmonale.[19, 20] The relative role of these two factors and the eventual level at which cardiac output will stabilize must await subsequent follow-up. Follow-up reports indicate clinically a progressive increase in exertional tolerance over the course of one to eight months at this writing, from which it is anticipated that the cardiac output gradually increases over the course of weeks and months.

4. *Pulmonary "capillary" pressure*: Since the valve orifice was enlarged and blood flow through it relatively unchanged, a striking fall of pulmonary "capillary" pressure occurred in eleven of the twelve patients (Figure 4). Baker, Brock, and Campbell[5] noted a fall of pulmonary arterial pressure post-operatively in three cases. The fall of pulmonary "capillary" pressure in our patients resulted in a relief of their pulmonary congestive symptoms which were their major cause of disability. In all but two cases, this pressure was well below the pulmonary edema level post-operatively. In W.F., pulmonary "capillary" pressure was little changed, but instead the cardiac output and blood flow through the valve had increased considerably. In A.D., severe mitral regurgitation was considered to be the cause of the failure of the pulmonary "capillary" pressure to fall to more normal levels. The dramatic fall of pulmonary "capillary" pressure post-operatively was reflected clinically by the impressive absence of dyspnea, orthopnea, and other signs and symptoms of pulmonary congestion in the post-operative period.

5. *Pulmonary arteriolar resistance*: In eight patients there was no significant change in pulmonary arteriolar resistance two to three weeks post-operatively (Figure 5). In E.L. and W.F., the decrease of resistance was striking and was in excess of any possible error in the methods. In T.C. and J.G., less striking but significant reductions of the resistance were observed. The marked fall of resistance in E.L. and W.F. so early in the post-operative period strongly suggests that part of the elevated arteriolar resistance pre-operatively was due to functional vasoconstrictor activity and that the post-operative values for resistance represented the residual obstruction due to organic narrowing of the arterioles which is known to be present in severe mitral stenosis.[13, 14] In two patients (B.A. and T.C.), values for resistance returned almost to normal (160 and 131 dynes second cm.-5 respectively) seven months post-operatively. Whether organic narrowing of pulmonary arterioles

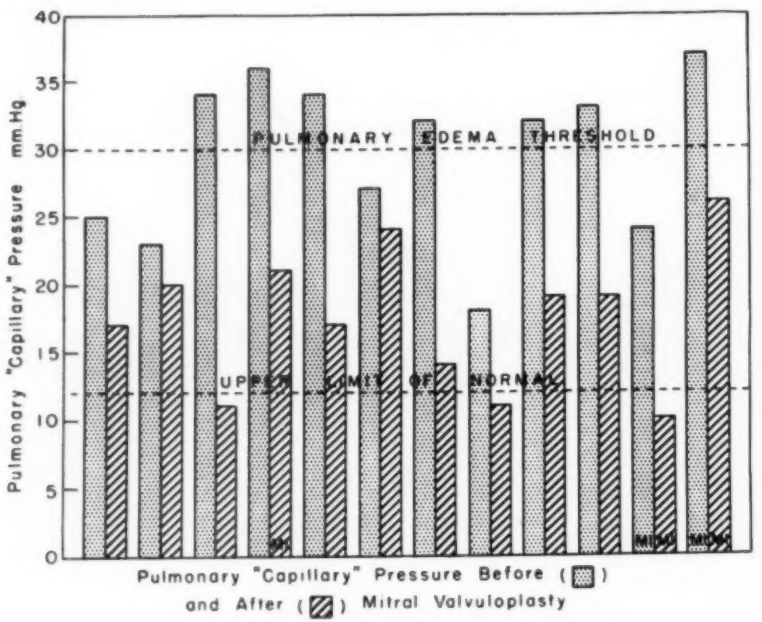
Pulmonary "Capillary" Pressure mm.Hg
40
35
30
25
20
15
10
5
0
PULMONARY EDEMA THRESHOLD
UPPER LIMIT OF NORMAL
Pulmonary "Capillary" Pressure Before ( )
and After ( ) Mitral Valvuloplasty

Fig. 4

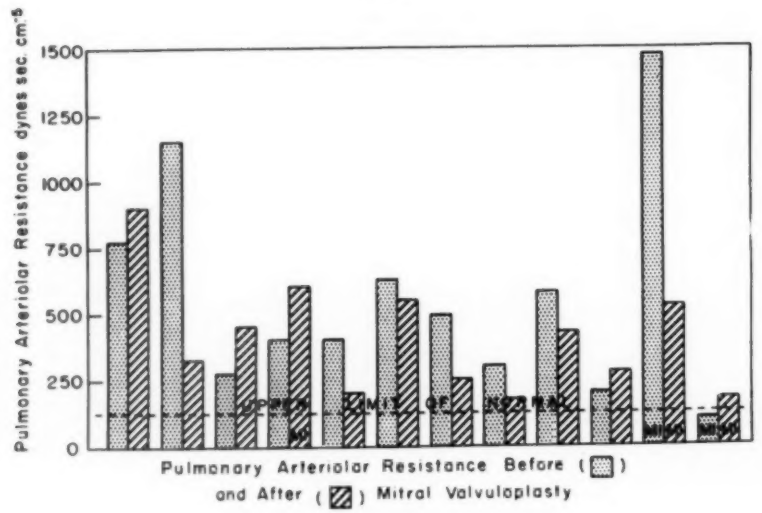
Pulmonary Arteriolar Resistance dynes sec. cm⁻⁵
1500
1250
1000
750
500
250
0
UPPER LIMIT OF NORMAL
Pulmonary Arteriolar Resistance Before ( )
and After ( ) Mitral Valvuloplasty

Fig. 5

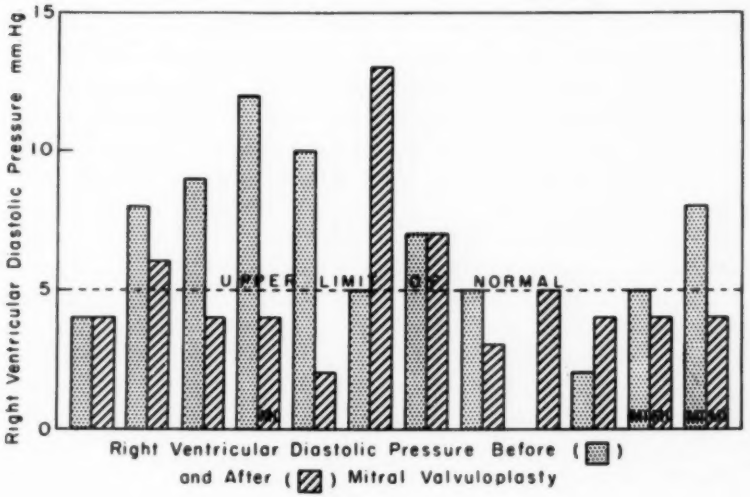

Fig. 6

is reversible in all patients is not known and must await study of more cases.

6. *Right ventricular function*: Six patients had elevations of right ventricular diastolic filling pressure (Figure 6). In four of these patients, values were normal post-operatively, in one (W.F.) it had fallen slightly, and in one (T.C.) it was unchanged. In one patient (L.L.) there was a rise from 5 mm. Hg pre-operatively to 13 post-operatively. Active rheumatic carditis was suspected as the cause, although there were no other confirmatory manifestations. The general trend was clearly a reversion toward but not necessarily to normal values early in the post-operative course.

Discussion

From these early post-operative observations, it is apparent that the surgical relief of mitral stenosis entails an evaluation not only of the stenotic valve itself, but also of mitral regurgitation, pressure and flow relations across the valve, arteriolar resistance in the lung, and right ventricular function.

The post-operative size of the mitral valve was increased in all cases

but was only 30 to 50 per cent of the normal size. By the surgical technique used, it seems unlikely to this author that the size can be made greater. As described in detail elsewhere,[11] a valve area of 1.5 sq. cm. or more should result in restoration to almost normal activity, assuming a regression of pulmonary vascular changes and return of right ventricular function to normal. If the valve is 2.0 sq. cm. or more, the patient has symptoms only on excessive exertion. A certain and appreciable number of such patients may never progress to symptomatic disease.[21] Surgery has certainly not been sufficiently perfected as yet to justify its use in patients with valve areas greater than 1.5 sq. cm.

A general concept in the past has been that relief of stenosis must be at the expense of producing mitral regurgitation. Harken[2] was the first to recognize that it was possible to relieve stenosis without producing regurgitation. The data reported here amply confirm him in demonstrating that the valve orifice can often be increased to a size which enables the patient to live a life of all but truly excessive activity without the concomitant production of regurgitation.

The early as well as later return of pulmonary arteriolar resistance toward normal in some of our patients is extremely encouraging and indeed surprising because authoritative pathological opinion has been that this would probably not occur.[14] Although relief of mitral valve obstruction would relieve pulmonary congestive symptoms, the patient might still remain relatively incapacitated if such elevated resistances persisted after operation.

The presence of auricular fibrillation in itself has no bearing on the decision to operate or not to operate. The incidence of embolism can be anticipated to be higher in fibrillators, but it is these very patients who stand to receive the greatest benefit from surgery. The eventual effect of the operation on cardiac rhythm remains to be determined. At this writing, there is no evidence that chronic auricular fibrillation spontaneously reverts to normal sinus rhythm post-operatively.

The only five absolute contraindications to operation at this stage of evolution of the surgical procedure, in our opinion, are: 1) that the mitral stenosis is too mild, i.e., symptoms are not severe enough to keep the patient from a useful and productive life; 2) that there is a serious associated disease, e.g., tuberculosis, nephritis, etc.; 3) that bacterial endocarditis is present; 4) that active rheumatic fever is present; and 5) that other valve lesions are present in serious degree. The recognition of rheumatic carditis is difficult when it is smouldering and often defies

all of the usual tests. If there are no clinical manifestations of rheumatic activity, however, it is assumed that rheumatic activity is either absent or so minimal as to be of little importance as regards the decision to operate.

Indications: In our opinion, tight mitral stenosis is *the* indication for mitral valvuloplasty. By tight is meant a valve area of 1.0 sq. cm. or less. This can usually be recognized accurately in patients with pure mitral stenosis without resorting to cardiac catheterization.

Mechanical narrowing of a mitral valve is well tolerated to a point. When it is but 20 per cent of its normal size, i.e., about 1.0 sq. cm., symptoms are present at rest or on the slightest exertion.[12, 22] We have encountered considerable difficulty in estimating larger valve sizes on clinical grounds alone, but have seldom had difficulty in recognizing "tight" mitral valves. In order to do this, aggravating factors must be eliminated such as thyrotoxicosis, pregnancy, active rheumatic carditis, subacute bacterial endocarditis, uncontrolled tachycardia, and other complicating episodes such as arterial or pulmonary embolism. In short, the patient is under good medical management without aggravating influences. The symptoms and signs derive from the mechanically obstructing mitral valve.

Nothing is so important as a careful history with one's attention focused on symptoms during the periods when these complicating events are *absent*, a careful physical examination, an x-ray and fluoroscopy of the heart, and an electrocardiogram. If the patient with pure mitral stenosis has any four of the following eight manifestations, he can be confidently assumed to have a mitral valve area of 1.0 sq. cm. or less, i.e., a tight mitral stenosis.[12]

1. Severe exertional dyspnea on one flight of stairs.
2. Left auricle moderately or markedly enlarged by fluoroscopy.
3. Pulmonary artery moderately or markedly enlarged by fluoroscopy.
4. Right ventricular hypertrophy by electrocardiogram.
5. Auricular fibrillation.
6. Heart 20 per cent or more enlarged by roentgenogram.
7. Hepatomegaly (4 cm. or more below the costal margin).
8. Three to four plus edema.

Four or more of these manifestations are, in our opinion, indications for mitral valvuloplasty.

The presence of mitral insufficiency or involvement of other valves in the rheumatic process complicates the decision regarding surgery.

It must be remembered that mitral valvuloplasty is designed specifically for relief of severe mitral stenosis. If other valves are involved, the degree of improvement from mitral valvuloplasty will not be so great as in pure mitral stenosis.

In patients with mitral stenosis, the estimation of the severity of other valve lesions is not easy. In our experience, the best clue to the *severity* of *aortic insufficiency* is the diastolic blood pressure; of *aortic stenosis*, the duration of systole on a brachial arterial pressure tracing; of *mitral insufficiency* the presence of left ventricular hypertrophy, combined ventricular hypertrophy, or even the absence of right ventricular hypertrophy in a patient with both systolic and diastolic murmurs at the apex whose symptoms and signs would lead one to expect that right ventricular hypertrophy ought to be present; of *tricuspid insufficiency* an enlarged pulsating liver; and of *tricuspid stenosis*, pronounced edema and ascites and an elevated venous pressure not responding well to the usual forms of cardiac therapy. Cardiac catheterization is now reserved for those cases which remain doubtful using the usual clinical measures. If one or more valves other than the mitral have serious disease, it is not in the best interest of the patient to operate. If one or more valves are minimally involved and the mitral valve is severely stenosed, a good but not excellent result from successful mitral valvuloplasty may be anticipated.

One of the pressing questions is whether the valve orifice will continue to remain patent for a prolonged period of time or whether it will become sealed off again in the course of weeks or months. Since the orifice is continually opening and closing, the only obvious ways in which it can become reduced in size again is by a recurrence of active rheumatic valvulitis or by thrombus formation on the fractured commissure at or shortly after operation, before endothelium has grown over the denuded areas. Sufficient objective data are as yet unavailable as regards the size of the mitral orifice six months or more after operation, but clinical follow-up on these patients indicates progressive improvement in their exercise tolerance over the course of the succeeding four to six months, which is possibly attributable to the regression of the secondary vascular changes in the lungs. After six months, their activity stabilizes and their capacity to exert themselves has shown no tendency to diminish. It would seem likely, then, that the valve orifice has remained unchanged in size for periods up to three years, which is the longest that any patients have been followed.

To date, 115 patients have had a finger fracture valvuloplasty performed by Dwight E. Harken. Sixty-five have been in his group 3[23] (corresponding with certain modifications to the same grouping of the New York Heart Association). There have been four operative deaths, a 6 per cent mortality – all in the earlier part of the series. Among fifty patients in group 4, there have been eighteen operative deaths, a mortality of 36 per cent. With experience and with the development of suitable instruments, there have been no technical deaths in the last eighty or more operations. Arterial embolism has accounted for seven deaths, cardiac standstill, ventricular fibrillation, and shock have accounted for about ten deaths, and the remainder have been from miscellaneous causes. Much of this mortality occurred during the developmental period of this type of surgery. Details of the surgical technique and anesthesia will be found in the publications of Harken.[16]

It is apparent that the operative risk is low in those patients who have pure mitral stenosis and who are incapacitated by exertional dyspnea, orthopnea, hemoptysis, and paroxysmal nocturnal dyspnea but whose hearts and livers are not greatly enlarged and who have little or no edema. In those who do have big hearts and signs of right ventricular failure, i.e., in those who are completely incapacitated, the risk is considerable, and the results are not so marked or so sure, but in some the benefit has been dramatic.

From this study, some of the problems of the effectiveness of mitral valvuloplasty have been answered, but many remain to be solved. The results are so encouraging, however, that this surgical approach seems to rest on solid ground.

Summary

1. The salient points of the pathological physiology and clinical manifestations of mitral stenosis and of surgical objectives are discussed.

2. Twelve patients with mitral stenosis on whom valvuloplasty was performed by Dr. D. E. Harken at the Peter Bent Brigham Hospital have been studied before and two to six weeks after operation in order to obtain objective information regarding the effectiveness of the surgical procedure.

3. The orifice of the mitral valve was increased in size in each case, but in none was it brought back to normal. In the majority, the postoperative size was such that normal but not excessive activity should be and actually was regained.

4. Mitral regurgitation was not produced in eleven of these twelve cases.

5. The immediate effect of operation in ten of twelve cases was to lower the pressure in the pulmonary circuit rather than to increase cardiac output.

6. In two patients, there was a dramatic decrease and in two others a significant decrease of pulmonary arteriolar resistance shortly after operation. In two, this resistance had returned to practically normal values seven months after operation. Whether changes in the arterioles of the lung will regress completely with the passage of time in all cases cannot be answered as yet.

7. There was a general tendency for the diastolic filling pressure of the right ventricle to decrease post-operatively to or towards normal.

8. Operative indications and risks are discussed.

The author is merely the spokesman for a team at the Peter Bent Brigham Hospital who have recently been concerned in the study of mitral stenosis.

Dr. Dwight E. Harken has performed the surgery, with the able assistance of Drs. R. E. Farrand, H. L. Black, and J. E. Dickson, III.

Without the collaboration and fundamental contributions to the pathological physiology and clinical and physiological correlations by Drs. R. Gorlin, B. M. Lewis, and F. W. Haynes, this work would not have been possible.

REFERENCES

1. Wilcox, L. D. and Grace, A. J. Barriers to surgery in mitral stenosis, *Congrès* (1) *Mondial de Chardiologie*, Paris 1950. Abstracts of papers, pp. 183-84.
2. Harken, D. E., Ellis, L. B., Ware, P. F. and Norman, L. R. Surgical treatment of mitral stenosis, *New Engl. J. Med. 239*:801-09, 1948.
3. Harken, D. E., Ellis, L. B. and Norman, L. R. Surgical treatment of mitral stenosis; progress in developing a controlled valvuloplastic technique, *J. Thorac. Surg. 19*:1-15, 1950.
4. Glover, R. P., O'Neill, T. J. E. and Bailey, C. P. Commissurotomy for mitral stenosis, *Circulation 1*:329-42, 1950.
5. Baker, C., Brock, R. C. and Campbell, M. Valvulotomy for mitral stenosis; report of six successful cases, *Brit. Med. J. 1*:1283-93, 1950.
6. Prip Buus, C. E. Traitement chirurgical des stenoses mitrales, 5 cas; film de l'operation. *Congrès* (1) *Mondial de Cardiologie*, Paris, 1950. Abstracts of papers, p. 187.
7. Dexter, L., Gorlin, R., Lewis, B. M., Haynes, F. W. and Harken, D. E. Physiological evaluation of patients with mitral stenosis before and after mitral valvuloplasty, *Trans. Amer. Clin. Climatol. Assoc. 62*:170-80, 1950.
8. Gorlin, R. and Gorlin, S. G. Hydraulic formula for calculation of the area of

the stenotic mitral valve, other cardiac valves, and central circulatory shunts, *Amer. Heart J. 41*:1-29, 1951.

9. Gorlin, R., Haynes, F. W., Goodale, W. T., Sawyer, C. G., Dow, J. W. and Dexter, L. Studies of the circulatory dynamics in mitral stenosis; altered dynamics at rest, *Amer. Heart J. 41*:30-45, 1951.
10. Gorlin, R., Sawyer, C. G., Haynes, F. W., Goodale, W. T. and Dexter, L. Effects of exercise on circulatory dynamics in mitral stenosis, *Amer. Heart J. 41*:192-203, 1951.
11. Gorlin, R., Lewis, B. M., Haynes, F. W., Spiegl, R. J. and Dexter, L. Factors regulating pulmonary "capillary" pressure in mitral stenosis, *Amer. Heart J. 41*:834-54, 1951.
12. Lewis, B. M., Gorlin, R., Houssay, H. E. J., Haynes, F. W. and Dexter, L. Clinical and physiological correlations in patients with mitral stenosis. *Amer. Heart J., in press.*
13. Parker, F., Jr. and Weiss, S. Nature and significance of the structural changes in the lungs in mitral stenosis, *Amer. J. Path. 12*:573-98, 1936.
14. Larrabee, W. F., Parker, R. L. and Edwards, J. E. Pathology of intrapulmonary arteries and arterioles in mitral stenosis. *Proc. Staff Meet. Mayo Clin. 24*:316-26, 1949.
15. Dexter, L., Dow, J. W., Haynes, F. W., Whittenberger, J. L., Ferris, B. G., Goodale, W. T. and Hellems, H. K. Studies of the pulmonary circulation in man at rest. Normal variations and the interrelations between increased pulmonary blood flow, elevated pulmonary arterial pressure, and high pulmonary "capillary" pressures, *J. Clin. Invest. 29*:602-13, 1950.
16. Harken, D. E., Dexter, L., Ellis, L. E., Farrand, R. E. and Dickson, J. L., III. Surgical treatment of mitral stenosis. Finger fracture valvuloplasty, *Ann. Surg. 134*:722-41, 1951.
17. Gorlin, R. and Dexter, L. Hydraulic formula for the calculation of the cross-sectional area of the mitral valve during regurgitation. *Amer. Heart J., in press.*
18. Gorlin, R., Lewis, B. M., Haynes, F. W. and Dexter, L. Studies of the circulatory dynamics at rest in mitral valvular regurgitation with and without stenosis. *Amer. Heart J., in press.*
19. Dexter, L.: Pulmonary circulatory dynamics in health and disease at rest, *Bull. New Engl. Med. Center 11*:240-46, 1949.
20. Dexter, L., Whittenberger, J. L., Gorlin, R., Lewis, B. M., Haynes, F. W. and Spiegl, R. J. The effect of chronic pulmonary disease (Cor Pulmonale and Hypoxia) on the dynamics of the circulation in man, *Trans. Assoc. Amer. Phys., 64*:226-35, 1951.
21. Sprague, H. B. and Carmichael, D. B., Jr. Rheumatic valvular disease in the aged, *Geriatrics 5*:239-51, 1950.
22. Gorlin, R. Physiologic and clinical correlations in mitral stenosis, *Bull. New Engl. Med. Center 13*:20-30, 1951.
23. Harken, D. E., Ellis, L. E., Dexter, L., Farrand, R. E. and Dickson, J. L., III. Responsibility of the physician in the selection of patients with mitral stenosis for surgical treatment, *Circulation, in press.*

SURGERY OF ACQUIRED VALVULAR DISEASE*

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INTRODUCTION

A CONSIDERATION of the surgery of acquired valvular disease at this moment involves principally the surgery of mitral stenosis. However, the surgical correction of aortic stenosis and insufficiency of the mitral valve is on the horizon, but at this time there is not enough evidence at hand to evaluate these procedures. Just beyond the horizon also are other techniques of dealing with acquired lesions of the cardiac valves, but these will await the further development of methods for carrying on the circulation artificially in order that one may operate under direct vision in a bloodless field.

HISTORY

At the beginning of this century the idea of surgically opening the stenosis of the mitral valve occurred to D. W. Samways[1] and Sir Lauder Brunton.[2] The latter had made the observation that the stenotic mitral valve could be opened readily at the time of autopsy and suggested that such an opening should be made in the slits of the valve and not across the leaflets. Thus in 1902 he wrote "On looking at the contracted mitral orifice in a severe case of this disease one is impressed by the hopelessness of ever finding a remedy which will enable the auricle to drive the blood in a sufficient stream through the small mitral orifice, and the wish unconsciously arises that one could divide the constriction as easily during life as one can after death. The risk which such an operation would entail would naturally make one shrink from it, but in some cases it might well be worthwhile for the patient to balance the risk of a shortened life against the certainty of a prolonged period of existence

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which could hardly be called life." It remained for Tuffier,[3] however, to make the first attempt at surgical correction of an acquired valvular lesion. In 1914 he reported improvement in the condition of a patient having aortic stenosis after digital dilatation of the aortic valve by invagination of the wall of the ascending aorta. The previous year, after an unsuccessful attempt to open a congenital stenosis of the pulmonary valve by introducing an instrument through the wall of the right ventricle, Doyen[4] considered using the same approach for relieving the stenosis of the mitral valve.

After this it was not until the 1920's that Cutler[5, 6] and his associates began an exhaustive experimental study of the problem. Their study led them to the surgical treatment of seven patients with mitral stenosis between the years of 1923-28. The approach to the problem was through the wall of the left ventricle using a valvulotome blindly – one of these patients survived. In 1923, Allen and Graham[7] attempted to relieve a stenosis of the mitral valve by means of a cardioscope which afforded some degree of visualization of intra-cardiac structures. In 1925 Pribram[8] in Germany using the technique of Cutler operated unsuccessfully upon a case of mitral stenosis. It is extremely interesting that Souttar[9] in England in the same year, using an approach through the auricular appendage, introduced his finger through the mitral valve successfully. This initial success, however, was not followed up and for the next eighteen years no further attempts were made. Of these twelve operations for mitral stenosis in this early period only three patients survived.

The renewed interest and present state of our knowledge of the surgery of acquired valvular disease is the result of the pioneering work of Bailey,[10] Harken[11] and Smithy.[12] The older methods of attack upon the mitral valve had relied for the most part upon excising or incising the stenotic valve to produce some degree of regurgitation through the valve as the cost of relieving the stenosis. Bailey's conception, which he has carried into practice, has been to incise the valve between the leaflets in the commissures to more normal tissue at the base of the valve to widely open the stenotic valve while preserving its function. Thus the stenosis is relieved without producing regurgitation back through the valve.

There is no difference of opinion now among the surgeons who have had the greatest experience in this field that the use of the left auricular appendage as the avenue of approach to the mitral valve is

far superior to any other technique. There is some question, however, as to the best method of separating the commissures of the stenotic mitral valve. Harken[13] is of the opinion that in most instances this separation can be adequately performed by finger manipulation which he calls finger fracture valvuloplasty. He reserves the technique of incising in the commissures for a minority of the cases. Blalock concurs with this practice. On the other hand Bailey[14] and his associates use an incision in the commissures in the majority of their cases because they believe that the division in the commissures is better controlled by this method and there is less likelihood of tearing into the valve leaflets which has the disastrous effect of producing an uncontrollable regurgitation. Also this group believes that a more adequate separation back to the normal tissues of the valve bases is made possible by an incision thus to insure better valve function with less likelihood of the recurrence of the stenosis.

Anatomy and Physiology of the Mitral Valve

For a complete understanding of the basic principles underlying these surgical maneuvers it is necessary to consider briefly the anatomic, pathologic and physiologic aspects of the mitral valve. The normal mitral valve is a somewhat conical cuff of thin flexible membrane. The apex and outer surface of the apical half of this cuff are attached by the numerous guy wires of the chordae tendineae originating in the papillary muscles which arise from the ventricular wall. The chordae tendineae are grouped more heavily in two areas of the apex of the mitral cuff thus forming two components of the valve, the antero-medial and postero-lateral leaflets. The base of the posterior leaflet is attached at the atrio-ventricular ring. The anterior or aortic leaflet is attached at its base to the ring surrounding the systemic aortic orifice and hence appears as a downward prolongation from the posterior border of the aortic orifice. This anatomical arrangement is extremely important because the large anterior leaflet is demonstrated as a baffle covering the mitral orifice and deflecting the flow of blood in systole through the aortic opening. Thus the large anterior leaflet is the main structure in protecting against marked regurgitation through the mitral valve and any interference with this function as a baffle against the aortic flow by operative tear or by disease will lead to compromising regurgitation.

The small posterior leaflet of the valve is of secondary importance

in the function of the mitral valve. Lying as it does along the lateral wall of the ventricle it is out of the line of the aortic thrust of blood in systole, but also because of this position it is displaced inward by the contraction of the ventricle thus permitting its leaflet to purse with the anterior leaflet to affect efficient closure of the valve.

The portions of the conical cuff which lie between the ends of the valves become infolded in the closure of the valves and it is these areas of infolding which become fixed in disease to produce an anatomic reality – the commissures.

In rheumatic disease with the fibrosis and contracture dependent upon it, the mitral valve becomes distorted. This distortion may be limited in extent and may resemble merely a purse string puckering of the valve orifice with the main portions of the leaflets remaining soft and pliable. In this instance where the valve orifice only is involved it is conceivable that the valve leaflets may close above the rigid stenotic opening to prohibit regurgitation. In other instances the disease involves greater portions of the cuff leaving a flexible margin only along its base. In far advanced disease the whole valve becomes a rigid, inflexible and often calcified plaque with a small ovoid fish mouth opening. In some of these latter instances where the valve leaflets are extensively involved and shortened, mitral regurgitation may be the predominating feature and surgical interference by manipulation of the valve is not indicated.

Surgical Technique

The technique of operation which has been employed on the First Surgical Division at Bellevue Hospital where Himmelstein, Lambert and the author have worked as a surgical team on this problem is fashioned closely after the techniques of Bailey and Harken from both of which it differs, but little.

The operation consists in a left lateral approach with the patient lying recumbent on the right side. The chest wall is opened widely in the 4th interspace by an intercostal incision extending posteriorly from the transverse processes of the vertebrae to the lateral border of the sternum anteriorly. A small incision is made in the pericardium and 5 cc. of 5 per cent novocaine is instilled and allowed to remain in the pericardial sac for five minutes with the incision clamped. The pericardium is then incised longitudinally 1 cm. anterior or posterior to the phrenic nerve depending upon the position of the underlying left auricular ap-

pendage. The left auricular appendage usually is distended and easily accessible. In four instances, however, the appendage has been the site of an organizing or organized thrombus. In two instances the auricular appendage thus involved appeared as a rudimentary process about the size of the tip of the index finger. After infiltration of the base of the auricular appendage with ½ per cent novocaine, a purse string suture of #1 braided silk is passed about the appendage at its base. A non-crushing clamp is closed over the base of the appendage and a portion of its tip is amputated. The right index finger is inserted in the left auricle as the clamp is released and the purse string suture drawn snugly about the finger. In the instances where the auricular appendage is rudimentary and obliterated, a modification of this technique entails passing the purse string suture about the appendage in the adjacent auricular wall and incising down within the wall of the obliterated appendage to gain access to the auricle. When the Bailey type knife is introduced with the finger, two gloves are worn on the operator's right hand. The blade of the commissurotomy guillotine knife is inserted between the gloves on the index finger – the tip of the outer glove having been removed and an opening made at the base of the index finger.

The finger is well tolerated in the auricle and exploration is carried out to find the mitral orifice. The size of the orifice is determined and an attempt is made to ascertain the site of the commissures. It is important to note at this time the presence or absence of a regurgitant jet coming back through the valve and to determine the extent of fibrosis and calcification involving the valve leaflets – particularly the antero-medial leaflet. If the disease has not involved this anterior leaflet it will be felt to bulge forcibly against the finger with each systole.

The finger is then forcibly introduced through the stenotic mitral orifice with pressure exerted in the direction of the antero-lateral commissure. In most instances the valve splits in the region of the commissures after the initial resistance of the fibrous ring at the mitral orifice. It has been our experience in a limited group that about 1/3 of the cases do not open widely by this method. In those instances, first where the valve cone is greatly elongated with a rubbery apperture and second where there is extensive fibrosis and calcification well back on the bases of the valve, one initial attempt is made to dilate, but if this fails the knife is employed. The knife is then protruded through the opening and the hooked blade engaged in the antero-lateral commissure. Ap-

proximation of the guillotine is carried out to divide the commissure. It has not seemed necessary in any of our cases to employ the knife in division of the postero-medial commissure.

The finger and knife are now withdrawn from the auricle as the purse string is tied. The cut edges of the auricular appendage are oversewn to insure closure. Several sutures are placed in the pericardial opening but no attempt at real closure is made. The chest is closed with intercostal tube drainage.

Selection of Patients for Operation

In the selection of cases for operation we have relied heavily as surgeons upon the judgment of our medical confreres Richards, Cournand, Ferrer and Harvey. I wish to emphasize here the value of close cooperation of a medical and surgical team in the selection and aftercare of these patients. It is obvious that all cases with stenosis of the mitral valve are not candidates for this operation. As experience accumulates, follow-ups on our patients become more adequate and the risk of operation in different groups better established, these indications will undoubtedly change.

At the present time, the group at Bellevue Hospital is of the opinion that the following are indications for a direct attack upon the stenotic mitral valve. Clinically, there should be symptoms and signs of pulmonary engorgement, dyspnea and cough on exertion, paroxysmal dyspnea, pulmonary edema or hemoptysis. In addition, supportive evidence of pulmonary hypertension and diminished output of blood from the left ventricle as a result of the block at the mitral valve is sought through cardiac catheterization studies in the digitalized patient. Elevated pressure in the pulmonary artery with a diminished cardiac output in the digitalized patient has been required as one criterion of acceptance of patients for commissurotomy.

Patients who give evidence of active rheumatic infection or of course, subacute bacterial endocarditis are not acceptable for operation. Also the presence of any major involvement of any of the other valves of the heart is at present a definite contraindication. Patients with a small degree of mitral regurgitation as evidenced by a systolic murmur have been considered for operation only where there was no evidence of left ventricular hypertrophy. Also minor aortic diastolic murmurs in the absence of other clinical evidence to support aortic insufficiency have not

been considered contraindications. Patients with a small degree of mitral regurgitation as evidenced by a systolic murmur have been considered for operation only where there was no evidence of left ventricular hypertrophy. Also minor aortic diastolic murmurs in the absence of other clinical evidence to support aortic insufficiency have not been considered contraindications. Bouts of frank cardiac failure have not been regarded as a deterrent to operation as long as the patient is compensated at the time of the procedure. Auricular fibrillation is not considered as of significance in the decision to operate.

It is our philosophy at the present time that it is more reasonable to accept the severely incapacitated patient for surgery where there is little doubt as to the progressive and crippling nature of the lesion than it is to accept those whose incapacity is only indicated in the future. This philosophy naturally carries with it a higher mortality as the more severe cases are encountered but at the present time the follow-up is not long enough to advocate the operation in those patients who are not definitely incapacitated or fail to show evidence of a definite degree of physiologic block as determined by cardiac catheterization studies. This attitude may be altered with the passage of time when more adequate follow-up will be available.

Results

A consideration of the results of this procedure should be focused first upon the immediate operative results in terms of mortality, second upon the early post-operative results in terms of a return to normal clinical activity with evidence of relief of the physiologic block at the mitral valve and third upon the long term follow-up where the problems of secondary contraction of the stenotic mitral valve and the effects of continued rheumatic activity will be answered.

A full evaluation of this procedure cannot be given until the answers to these last problems are known. In the meantime, the evidence at hand indicates that the mortality of the operation and the early results in properly selected cases certainly justify the continued use of this operation. Whereas the initial mortality reported on the first small groups of patients operated upon by Harken and Bailey was 60 per cent, the development of technique and better selection of patients has brought the mortality down to nearer 10 per cent in these experienced hands. Alfred Blalock[15] has recently reported two deaths in a series of twenty-

five cases. In one of the patients that died, intracardiac manipulation was not performed because of the obliteration of the auricular appendage and death was due to cerebral embolism. Naturally the mortality will fluctuate with the severity of the disease but where selection of the patients has been strict the chance of improvement at present well justifies the risk.

What are the early results and what are some of the limitations that are recognized? At the present time there is little statistical evidence even on the early results in these patients. Glover[16] has reported for Bailey's group on 41 patients on whom commissurotomy was performed. Twenty of these or approximately 50 per cent are considered to be excellent results from the clinical standpoint. The remainder, or 21, they consider to be improved. In this respect our experience, although small, is worth reciting. Nine patients between the ages of twenty-six and forty-nine years have been accepted for this operation and seven have survived. One of these patients died at operation when the posterior wall of the auricle ruptured as the finger was being introduced through the auricular appendage. The other had a cardiac arrest during intracardiac manipulation and although normal rhythm was re-established by cardiac massage, the patient did not regain consciousness and died eighteen hours later.

The status of the seven survivors is as follows: five of these patients are, from a symptomatic point of view, considered as excellent early results and two are classified as improved at the present time. Of the five patients who are considered to be in the excellent category, two who were operated upon nineteen and sixteen months ago have had cardiac catheterization studies one year following surgery. These studies now add the weight of laboratory evidence to that of the clinical, and also show that there seems to be continuous improvement in these patients. The status at one year following operation is better than at one month after surgery from the evidence of these data.

Of the two patients who are considered improved symptomatically at this time, one we believe will prove to be our poorest result. There was a mild degree of regurgitation through a stenosed calcified mitral valve in this case. The degree of regurgitation was not lessened by incising the commissure anteriorly to relieve the stenosis, because of the immobility of the leaflets. Also the histologic examination of the auricular appendage showed active rheumatic auriculitis in spite of no evidence

of clinical activity during a long period of observation prior to operation. Although auriculitis has been found in three other of our patients we believe that it is significant in this case because of a prolonged febrile course post-operatively. Thus, in the early follow-up, rheumatic activity although unsuspected clinically, is actually shown to be present in some of these patients and may act as a limiting factor.

Another factor which may alter the result obtained from mitral commissurotomy is the secondary obstruction in the pulmonary circuit due to pulmonary atherosclerosis in long standing cases of mitral stenosis. Julian Johnson[17] has drawn attention to this and believes that the obstruction due to pulmonary vascular lesions in some cases may be significant enough to negate the effect of surgical opening of the mitral valve. Our group is investigating this aspect of the problem but as yet has no evidence of a convincing nature.

A complication has occurred in two of our patients during the period of six weeks to four months following operation. This has consisted in recurring attacks of fever and bilateral chest pain without cough lasting from five days to a week. The explanation of these episodes is not clear at the present time. With them there has been no evidence of cardiac decompensation although in one case auricular fibrillation was present transiently. It is surmised that these attacks may represent rheumatic activity, possibly a pericarditis. However there has been no evidence either by x-ray or by electrocardiography to substantiate that diagnosis.

As has been suggested in this review of the early follow-up in a small group of patients there are a number of factors such as the effect of continued rheumatic activity and pulmonary arteriosclerotic changes which will have to await a longer close follow-up for a proper evaluation. Subsequent observations also may show that there is a gradual reformation of the stenosis either with or without recurring rheumatic activity. However, the early results that are being obtained in the treatment of mitral stenosis by a direct attack on the valve are good, and we believe, far outweigh the risk of the operation in carefully selected patients.

Pulmonary Edema in Mitral Stenosis

In addition to the method of treating mitral stenosis by direct attack upon the valve, efforts have been made to prevent the bouts of pul-

monary edema which occur in this disease. Attempts to solve this problem have been made by the anastomosis of systemic and pulmonary veins as performed by Sweet.[18] Harken[19] also has suggested the making of an inter-auricular defect to alleviate bouts of pulmonary edema. The utility of any such shunting procedures must be limited. In a well marked mitral stenosis there is a diminished outflow of blood from the left ventricle and there is an inability to increase this output with exercise. Therefore any decrease in the amount of blood reaching the left ventricle, as might occur in the production of a shunt, will not be tolerated. It seems clear now that any indirect surgical attack on the problem of mitral stenosis is inferior to that of removing the crucial block in the circulation by surgical opening of the stenotic area itself.

Mitral Insufficiency

The surgical correction of insufficiency of the mitral valve is distinctly in the experimental stage of development. Investigation of this problem has been directed in the main along three lines. First, ingenious mechanical plastic valves have been anchored in place in experimental animals. It is certainly possible that such mechanical valves could be introduced and secured in the diseased valves of humans by the same techniques, but it is very doubtful that these valves would continue to function for any extended period of time.

Second, efforts have been made to repair experimental defects in valves using tissue grafts. Gordon Murray[20] used inverted segments of vein and Templeton and Gibbon[21] vein and pericardial grafts to accomplish this feat in animals. Although the fate of these grafts has been somewhat encouraging, it is highly improbable that such grafts would flourish in the scarred areas of diseased valves.

The third line of endeavor in the correction of the insufficiency of the mitral valve has been directed towards the use of pedicled flaps placed across the left ventricle just below the mitral valve so that the flap will obstruct the incompetent valve in systole. Gordon Murray[22] has used vein segments while Bailey has employed pericardial grafts to achieve the same purpose. It is impossible at this time to give a proper evaluation of this method. It is fair to say that the problem of insufficiency of the valves of the heart is going to be a difficult one to solve because of the complicated mechanism of the valve function.

Aortic Stenosis

Aortic stenosis is another acquired valvular lesion which is challenging the ingenuity of investigators in this field. It is extremely interesting to recall that the first successful operation for an acquired valvular lesion was performed in 1914 by Tuffier.[3] As has been noted previously he was able to invaginate the wall of the ascending aorta through the stenosed aortic opening using his finger and apparently to widen the stenotic area as the patient was living ten years later. Investigation of the possibility of treating this lesion surgically was revived by the late Horace Smithy[12] in the 1940's. Incision of the stenotic aortic valve using the left ventricular approach has been performed by Blalock and by Bailey but without success. The problem of opening the stenotic aortic valve is not only complicated by the difficulty of approach, but also the production of appreciable degree of regurgitation is not tolerated.

More recently Bailey and his associates have attempted to stretch the stenotic aortic valve using a dilator instead of an instrument to incise the valve, with more success. Originally an approach was made through the carotid artery and down the aorta, but apparently this route has now been abandoned in favor of the ventricular approach. It is only possible now to indicate the methods that are being employed to attack the complicated problems involved in the solution of insufficiency of the mitral valve and of stenosis of the aortic valve. It is probable that even now there are other methods under investigation which will solve these complicated surgical problems. On the other hand it may be that the solutions will not be found until operations can be performed in a dry field under direct vision—which means the perfection of a technique of extracorporal circulation.

At this time in the mid-stream of progress in the field of acquired valvular surgery it is possible to state that the operation for mitral stenosis is of great benefit to a selected group of patients with this disease. The future with an adequate follow-up of these cases will prove whether these patients are permanently cured or whether they have been given worthwhile respite from the continued ravages of rheumatic disease.

[*REFERENCES ON NEXT PAGE*]

REFERENCES

1. Samways, D. W. Cardiac peristalsis; its motion and effects, *Lancet 1*:927, 1898.
2. Brunton, L. Preliminary note on possibility of treating mitral stenosis by surgical methods, *Lancet 1*:352, 1902; and Surgical operation for mitral stenosis, *ibid. 1*:547, 1902.
3. Tuffier, T. État actuel de la chirurgie intrathoracique, *Trans. 17th int. Congr. Med. 11*:249; 326, 1913-1914.
4. Doyen, E. Chirurgie des malformations congenitales ou acquises du coeur, *Ann. Med. 21*:86, 1913.
5. Cutler, E. C., Levine, S. A. and Beck, C. S. The surgical treatment of mitral stenosis; experimental and clinical studies, *Arch. Surg. 9*:680-821, 1924.
6. Cutler, E. C. and Beck, C. S. Present status of surgical procedures in chronic valvular disease of the heart; final report of all surgical cases, *Arch. Surg. 18*:403-16, 1929.
7. Allen, D. S. and Graham, E. A. Intracardiac surgery; a new method, *J. Amer. med. Assoc. 79*:1028-30, 1922.
8. Pribram, E. O. Die operative Behandlung der Mitralstenose, *Arch. klin. Chir. 142*:458-65, 1926.
9. Souttar, D. W. Surgical treatment of mitral stenosis, *Brit. med. J. 2*:603-06, 1925.
10. Bailey, C. P. Surgical treatment of mitral stenosis (mitral commissurotomy), *Dis. Chest 15*:377-93, 1949.
11. Harken, D. E., Ellis, L. B., Ware, P. F. and Norman, L. R. Surgical treatment of mitral stenosis, *New Engl. J. Med. 239*:801-09, 1948.
12. Smithy, H. G. and Parker, E. F. Experimental aortic valvulotomy, *Surg. Gynec. Obstet. 81*:625-28, 1947.
13. Harken, D. E., Ellis, L. R. and Norman, L. R. Surgical treatment of mitral stenosis; progress in developing a controlled valvuloplastic technique, *J. thorac. Surg. 19*:1-15, 1950.
14. Bailey, C. P., Glover, R. P. and O'Neill, T. J. E. Surgery of mitral stenosis, *J. thorac. Surg. 19*:16-45, 1950.
15. Blalock, A. Consideration of some of the problems of cardiovascular surgery, *J. thorac. Surg. 21*:543-71, 1951.
16. Glover, R. P., Bailey, C. P. and O'Neill, T. J. E. Surgery of stenotic disease of the heart, *J. Amer. med. Assoc. 144*: 1049-57, 1950.
17. Welch, J., Johnson, J. and Zinsser, H. Significance of pulmonary lesions in the selection of patients for mitral valve surgery, *Ann. Surg. 132*:1027-34, 1950.
18. Sweet, R. H. and Bland, E. F. Surgical relief of congestion in the pulmonary circulation in cases of severe mitral stenosis, *Ann. Surg. 130*:384-97, 1949.
19. Ellis, L. B. and Harken, D. E. Mitral stenosis, clinico-physiologic correlations with particular reference to surgical intervention, *Trans. Amer. clin. climat. Assoc. 60*:59-70, 1948.
20. Murray, G., Wilkinson, F. R. and MacKenzie, R. Reconstruction of the valves of the heart, *Canad. med. Assoc. J. 38*: 317-19, 1938.
21. Templeton, J. Y., III and Gibbon, J. H., Jr. Experimental reconstruction of cardiac valves by venous and pericardial grafts, *Ann. Surg. 129*: 161-76, 1949.
22. Murray, G. Surgical treatment of mitral stenosis, *Canad. med. Assoc. J. 62*:444-47, 1950.

STATEMENT CONCERNING STATE EDUCATION LAW

At the close of the 1950 session, the New York State Legislature passed an amendment to the State Education Law which permits pupils to be excused from the study of health and hygiene if their parents or guardians object to this instruction on the ground that it conflicts with the tenets of their religion.

This amendment has become a part of the law of the State. In accordance with the new statute, the Department of Education has directed school principals to excuse children of the Christian Science faith from courses dealing with health subjects if their parents or guardians so request. Moreover, the Department of Education has indicated that "Required sections of the Regents' examination as well as the State Scholarship examinations will be constructed so as not to penalize pupils who have been excused from instruction in the specified units of study."

Teachers of the biological sciences report that the application of this law creates numerous difficulties. It disrupts the orderly teaching of biology and hygiene, the basis of modern sanitation and public health. It may prove to be an obstacle to college entrance not only for Christian Scientists but for all pupils, who may be inclined to neglect the biological sciences related to public health because these subjects are excluded from examinations.

The whole structure of protective procedures against smallpox, yellow fever, diphtheria and many other communicable diseases, and the safeguarding of our water and milk as well as other foods rests on well established biological facts. Such facts must be made known to every school child for proper orientation in natural and social phenomena. Ignorance of the reasons for community action in the field of scientific and public health procedures is a potential source of danger to the community. A sound training in the fundamentals of the biological sciences is essential to an understanding of the principles underlying the rules of personal hygiene and of public health.

Generally accepted scientific knowledge should be part of our children's educational heritage, and no one should deprive them of it. The very fact that some pupils are excused from the acquisition of essential knowledge and from answering questions pertaining to it is likely to have a bad effect on others; it tends to lower the level of health and hygiene teaching throughout the State. It is unsound to permit any group to interfere with the progress of education, especially the teaching of the fundamentals of biology and of public and personal hygiene. The restriction imposed by this amendment is particularly unfortunate at a time when the nation is straining its potentialities to the utmost to organize its material and human resources to defend its very existence.

In the interest of sound education and the protection of the public health and welfare, The New York Academy of Medicine urges the repeal of this amendment to the Education Law.

December 10, 1951.

* Issued by The Committee on Public Health Relations of The New York Academy of Medicine.

RECENT ACCESSIONS TO THE LIBRARY

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Northwestern University. Medical School. A review of medicine by members of the faculty. 6.ed. edited by B. Boshes. Chic., [Chief Print. Co.], 1951, 814 p.

Olivier, H. R. Examens de laboratoire. Paris, Maloine, 1950, 200 p.

O'Rourke, J. T. Oral physiology [mastication]; edited by L. M. S. Miner. St. Louis, Mosby, 1951, 333 p.

Partridge, M. A. Pre-frontal leucotomy; a survey of 300 cases personally followed over 1½-3 years. Oxford, Blackwell, [1950], 496 p.

Pascal, G. R. & Suttell, B. J. The Bender-Gestalt test; quantification and validity for adults. New York, Grune, 1951, 274 p.

Peck, S. M. & Klein, G. Therapy of dermatologic disorders. Phila., Lea, 1951, 383 p.

Petrovskiy, B. V. Khirurgicheskoe lechenie raka pishchevoda i kardii. [Surgical treatment of cancer of the oesophagus and the cardia.] Moskva, Izd. Akad. Med. Nauk SSSR, 1950, 169 p.

Philps, A. S. Ophthalmic operations. London, Baillière, 1950, 397 p.

Pichler, H. Lehrbuch der Kavitätenpräparation nach des Grundsätzen G. V. Blacks. 2.Aufl. Leipzig, Barth, 1949, 120 p.

Pistor, H. Die Methoden der objektiven Refraktionsbestimmung mit dem einfachen Augenspiegel. Stuttgart, Weinbrenner, 1948, 95 p.

Pizon, N. P. Radiodiagnostic obstétrical. [Paris], Expansion Scientifique Française, 1948, 161 p.

Pochon, J. J. L. & Tchan, Y. Précis de microbiologie du sol. Paris, Masson, 1948, 222 p.

Portmann, G. Thérapeutique médicale oto-rhino-laryngologique. Paris, Doin, 1950, 315 p.

Pratt, R. & Youngken, H. W. Pharmacognosy; the study of natural drug substances and certain allied products. Phila., Lippincott, [1951], 644 p.

Querschmitt (Ein) durch die Arbeit der Tübinger Nervenklinik. Ernst Kretschmer zum sechzigsten Geburtstag von seinen Schülern und Mitarbeitern. Berlin, Springer, 1949, 420 p.

de Quervain, F. Spezielle chirurgische Diagnostik. 10.Aufl. neubearb. von Karl Lenggenhager. Berlin, Springer, 1950, 767 p.

Quick, A. J. The physiology and pathology of hemostasis. Phila., Lea, 1951, 188 p.

Race, R. R. & Sanger, R. Blood groups in man. Oxford, Blackwell, [1950], 290 p.

Radiochemical studies; the fission products. Edited by C. D. Coryell & N. Sugarman. New York, McGraw-Hill, 1951, 3 v.

Ramon, G. Le principe des anatoxines et ses applications. Paris, Masson, 1950, 229 p.

Read, G. D. Introduction to motherhood. London, Heinemann, 1951, 92 p.

Reading, P. V. Common diseases of the ear, nose and throat. London, Churchill, 1950, 288 p.

Reese, A. B. Tumors of the eye. [New York], Hoeber, [1951], 574 p.

Regenbogen, E. Diagnostische und therapeutische Eingriffe des Internisten. Stuttgart, Thieme, 1949, 262 p.

Ritvo, M. Chest X-ray diagnosis. Phila., Lea, 1951, 558 p.

Rolin, J. Drogues de police. Paris, Plon, [1950], 306 p.

Rothschild, F. S. Das Ich und die Regulationen des Erlebnisvorganges. Bâle, Suisse, Karger, 1950, 388 p.

Rozanov, B. S. Profuznye jeludochnye krovotecheniya yazvennogo kharaktera i ikh khirurgicheskoe lechenie [Profuse

stomach haemorrhage from ulcers and its surgical treatment.] Moskva, MEDGIZ, 1950, 137 p.

Rozental, A. S. Khronicheskaya rasstroystva pitaniya i pishchevareniya v rannem detskom vozraste. [Chronic alimentary and digestive disorders in young children.] Moskva, Izd. Akad. Med. Nauk SSSR. 1948, 294 p.

Ruesch, J. & Bateson, G. Communication: the social matrix of psychiatry. New York, Norton, [1951], 314 p.

Russ, S.; Clark, L. H. & Pelc, S. R. Physics in medical radiology. London, Chapman, 1950, 296 p.

Sarradon, P. Le docteur Laënnec. Paris, Laffont, [1949], 190 p.

Schinz, H. R. Vom Krebs und seiner Bekämpfung. Zürich, Beer, 1949, 93 p.

Schunck de Goldfien, J. Anthropotechnie médicale. Paris, Maloine, 1950, 189 p.

Schweitzer, J. M. Oral rehabilitation. St. Louis, Mosby, 1951, 1161 p.

Seitz, W. & Ballowitz, K. Die Infektionskrankheiten; ihre Entstehung und ihre Behandlung. 2.Aufl. Berlin, Urban, 1948, 320 p.

Seymour, F. I. Rice, dietary controls and blood pressure, with menus and recipes. New York, Froben Press, 1951, 206 p.

Simons, B.; Nöller, F. & Busse, E. Dringliche Operationen bei Schussverletzungen. Stuttgart, Piscator, 1949, 506 p.

Smillie, I. S. Injuries of the knee joint. 2. ed. Edinburgh, Livingstone, 1951, 391 p.

Soffer, L. J. Diseases of the endocrine glands. Phila., Lea, 1951, 1142 p.

Sors, C. Les broncho-pneumopathies segmentaires chez l'enfant et chez l'adulte. Paris, Foucher, [1950], 255 p.

Soulas, A. & Mounier-Kuhn, P. L. Bronchologie; technique endoscopique et pathologie trachéo-bronchique. Paris, Masson, 1949, 653 p.

Spear, M. R. Keeping idle hands busy; occupational therapy. Minneapolis, Burgess, [1950], 96 p.

Stallard, H. B. Eye surgery. 2.ed. Bristol, Wright, 1950, 667 p.

Steger, M. Hypnoidal psychotherapy. New York, Froben Press, 1951, 150 p.

Stekel, W. Technique of analytical psychotherapy. [Rev.ed.]. London, Bodley Head, [1950], 403 p.

Sutcliffe, A. & Canham, J. W. The heights and weights of boys and girls. London, Murray, [1950], 80 p.

Syndrome (Le) hépato-ovarien, [par] J. A. Huet [et al.]. 2.éd. Paris, Expansion Scientifique Française, 1950, 101 p.

Teleky, L. Die Entwicklung der Gesundheitsfürsorge — Deutschland, England, USA. Berlin, Springer, 1950, 142 p.

Terhune, W. B. The integration of psychiatry and medicine; an orientation for physicians. New York, Grune, 1951, 177 p.

Terracol, J.; Corone, A. & Guerrier, Y. La trompe d'Eustache. Paris, Masson, 1949, 218 p.

Teschendorf, W. Lehrbuch der röntgenologischen Differntialdiagnostik. 2.Aufl. Suttgart, Thieme, 1950, 2 v.

Therapeutics in internal medicine, edited by F. A. Kyser. N. Y., Nelson, [1950], 715 p.

Thoma, K. H. Oral pathology. 3.ed. St. Louis, Mosby, 1950, 1592 p.

Thomas, J. E. The external secretion of the pancreas. Springfield, Ill., Thomas, [1950], 149 p.

Toulant, M. Manifestations oculaires des trypanosomiases humaines. Paris, Masson, 1950, 103 p.

Tournay, R. & Wallois, P. Les varices de la grossesse et leur traitement principalement par les injections sclérosantes. Paris, Expansion Scientifique Française, 1948, 139 p.

Tourneur, R. & Contamin, F. Dossier de pathologie médicale pour l'Internat des hôpitaux de Paris. Paris, Bertrand, 1949-1951, 2 v.

Tur, A. F. Gematologiya detskogo vozrasta. [Haematology in childhood.] Moskva, Izd. Akad. Med. Nank SSSR, 1950, 274 p.

Ugolino da Montecatini. Tractatus de balneis. Trascrizione, traduzione italiana . . . a cura del prof. M. G. Nardi. Firenze, Olschki, 1950, 143 p.

United States. Army. Evacuation Hospital no. 77. Medicine under canvas; a war journal [of the University School of Medicine hospital unit]. Kansas City, Mo., Sosland, [1949], 196 p.

United States. National Cancer Institute. Cancer services and facilities in the United States, 1950. [Wash., U. S. Govt. Print. Off., 1950], 152 p.

United States. Public Health Service. Division of Industrial Medicine. Industrial health and medical programs. Wash., U. S. Govt. Print. Off., 1950, 397 p.

United States. Surgeon General's Committee on Medical School Grants and Finances. Medical school grants and finances. [Wash., U. S. Govt. Print. Off., 1951], 3 pts. in 1 v.

University of Minnesota. Center for Continuation Study. Continuation course in otolaryngology, June 26-30, 1950. Minneapolis, [1950], 62 numb. leaves.

Vagliano, M. S. La gelure; étude clinique. Paris, Masson, 1948, 255 p.

Veterans Administration Conference on Cortisone Research, Wash., 1950. A symposium. Rahway, N. J., Merck, [1951], 120 p.

Vignes, H. Eclampsie et éclampsisme. Paris, Masson, [1948], 217 p.

Voronin, L. G. Analiz i sintez slojnykh razdrajiteley normalnymi i povrejdennymi polushariyami golovnogo mozga sobaki; pod redaktsiey L. A. Orbeli. [Analysis and synthesis of complex irritations in normal and injured cerebral hemispheres of dogs; edited by L. A. Orbeli.] Moskva, Izd. Akad. Med. Nauk SSSR, 1948, 263 p.

Voss, O. E. A. Pyramideneiterungen; deren Verhütung und Behandlung. Stuttgart, Thieme, 1949, 256 p.

Vossschulte, K. Grundlagen der Schmerzbekämpfung durch Sympathikusausschaltung. Berlin, Urban, 1949, 132 p.

W. K. Kellogg Foundation, Battle Creek, Mich. An experience in health education. Battle Creek, Mich., W. K. Kellogg Foundation, 1950, 175 p.

Walker, K. M. A doctor digresses. London, Cape, [1950], 207 p.

Warburg, O. Heavy metal prosthetic groups and enzyme action. Oxford, Clarendon, 1949, 230 p.

Weber, A. Die Elektrokardiographie und andere graphische Methoden in der Kreislaufdiagnostik. 4.Aufl. Berlin, Springer, 1948, 209 p.

Whitacre, F. E. & Jones, E. W. Maternity care in two counties: Gibson County, Tennessee; Pike County, Mississippi, 1940-41, 1943-44. N. Y., Commonwealth Fund, 1950, 165 p.

Williams, L. H. W. Aids to obstetrics. 12. ed. London, Baillière, 1949, 254 p.

Willis, R. A. The principles of pathology. London, Butterworth, 1950, 667, 55 p.

Wishnefsky, N. Antihistamines; industry and product survey. N. Y., Chemonomics, 1950, 157 p.

Wyburn-Mason, R. Trophic nerves; their role in physiology and pathology. London, Kimpton, 1950, 1083 p.

CLINICAL RESEARCH MEETING

The New York Academy of Medicine will hold meetings Wednesday and Thursday evenings, April 23 and 24, 1952, at which investigators of New York City and vicinity may present results of original research in Clinical Medicine.

This meeting is being arranged by the Committee on Medical Education of the Academy with the following stipulations:

1) Presentations will be confined to original research in clinical medicine or surgery, or to research which is applicable to medicine or surgery in all clinical branches.

2) Preference will be given to papers which have not been presented before a national or local society (other than intramural).

3) In submitting application, the investigator is requested to state whether this work has been published or has been submitted for publication; also, in cases where the investigator is working under the head of department of a hospital or research institute, approval of the head of department should accompany the application.

Presentations will be limited to twelve minutes. A brief period of free discussion will follow each presentation.

The publication of presentations is not a necessary condition but the Academy plans to publish promptly abstracts of presentations, if the author so desires. In order to expedite publication of *abstracts*, the Committee requests that the abstract submitted by the investigator be carefully prepared in the form in which publication is desired, with the understanding that publication of the abstract in the Bulletin shall not preclude publication by the author in any other journal.

The Committee extends an invitation to all research workers of Greater New York and of neighboring cities within a radius of one hundred miles to submit *an abstract of proposed presentation in QUADRUPLICATE*, not to exceed five hundred words in length, to the Secretary of the Committee on Medical Education of the Academy, Dr. Robert L. Craig, *not later than February 15, 1952*. A formal invitation to participate in this program will then be extended by the Committee to the authors of papers selected for presentation.

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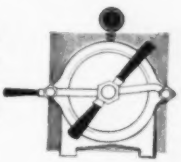

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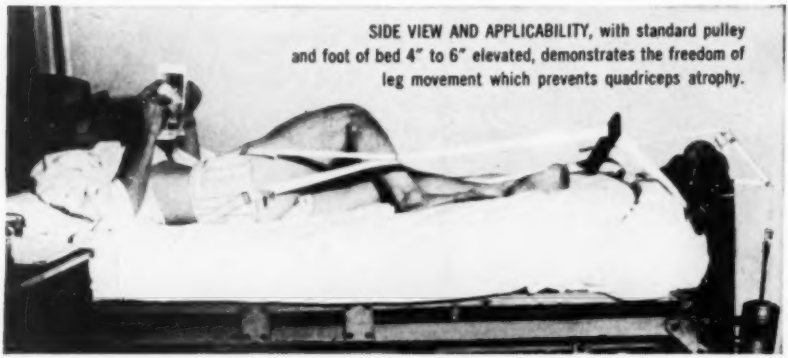

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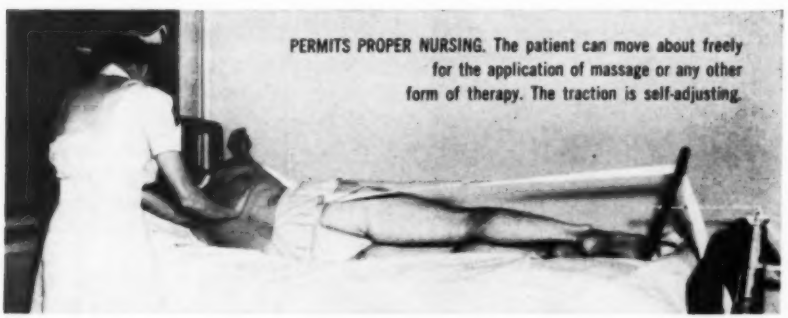

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1. Heimer, C. B., Grayzel, H. G., and Kramer, B.: Archives of Pediat. 68:382, 1951.
2. Behrman, H. T., Combes, F. C., Bobroff, A. and Leviticus, R.: Ind. Med. & Surg. 18:512, 1949.

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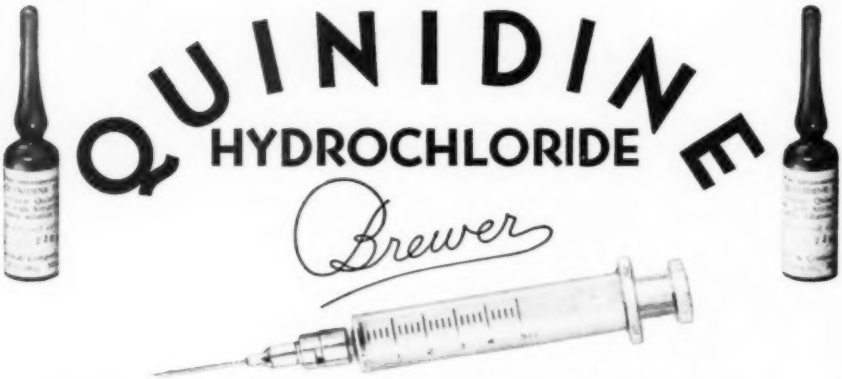

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1. Sturnick, M. I.; Riseman, J. E. F.; and Sagall, E. I.: Studies on the Action of Quinidine in Man: J. A. M. A. 121; 917 (March 20) 1943
2. Sagall, E. I.; Horn, C. D.; and Riseman, J. E. F.: Studies on the Action of Quinidine in Man: Arch. Int. Med. 71; 460 (April) 1943
3. Armbrust, Chas. A. Jr. and Levine, Samuel A.: Paroxysmal Ventricular Tachycardia: A Study of 107 Cases: Circulation, 1; 28-39 (Jan.) 1950
4. Bell, G. O.; Bradley, R. B.; and Hurxthal, L. M.: Paroxysmal Tachycardia, Experiences with Massive Doses of Quinidine Intravenously in a Refractory Case: Circulation, 1; 939 (April Part II) 1950

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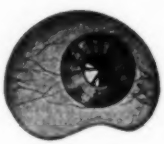

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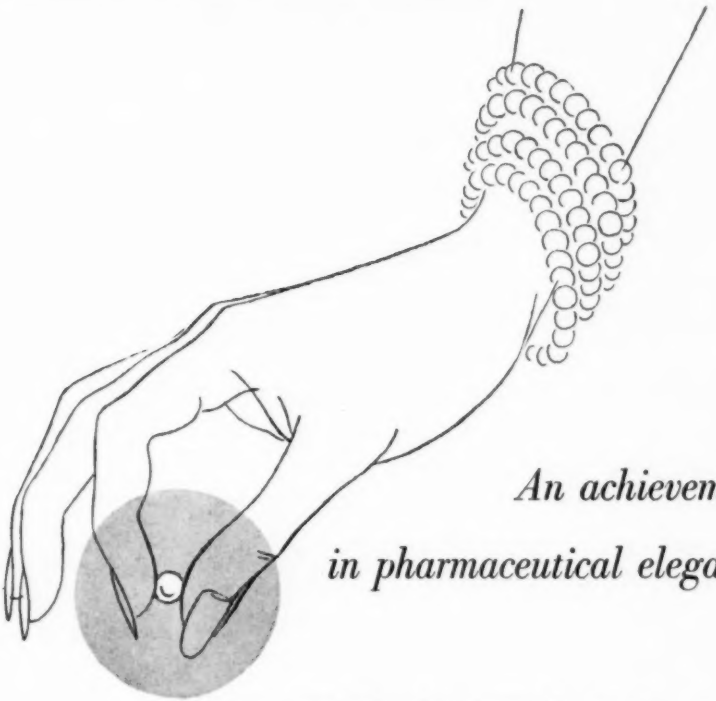

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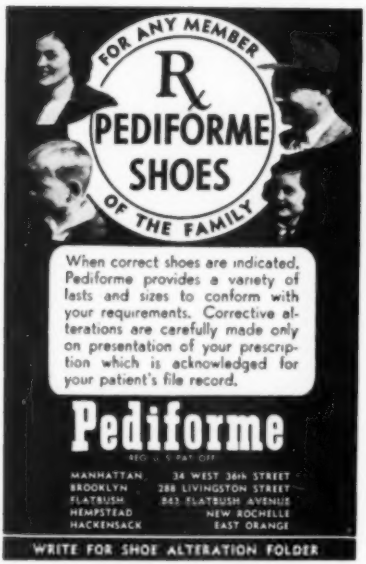
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Dowd, George; Rehabilitation of the Arteriosclerotic Worker: Medical Times, June 1951. Morrison, L. M.; J. A. M. A., April 21, 1951.

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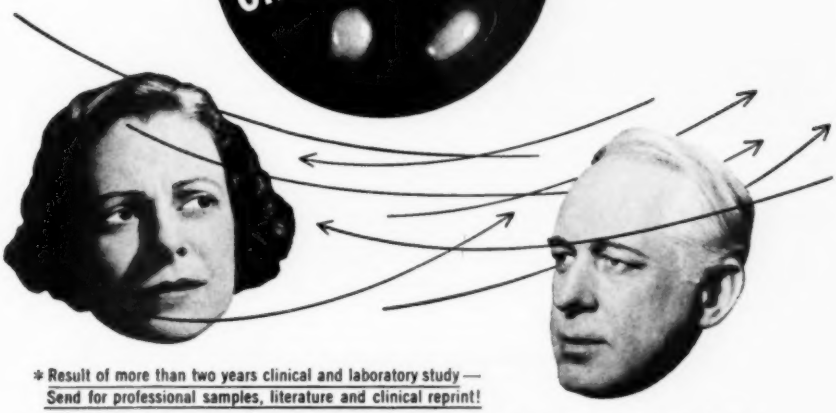

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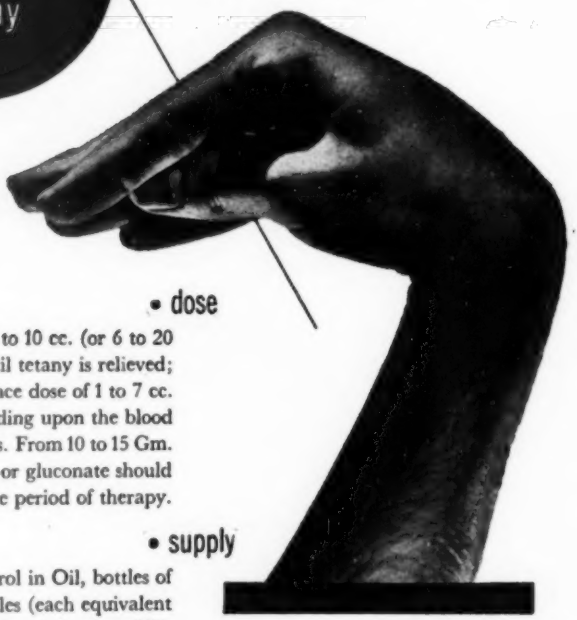

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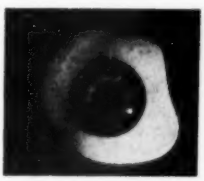

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Mull-Soy is the nutritional replacement of choice for patients, *young or old*, who display a true allergy to animal milks. Mull-Soy supplies (in standard 1:1 dilution) essential protein, fat, carbohydrate and minerals in values comparable to those of cow's and goat's milk. The fat in Mull-Soy is soy oil which is a good source of unsaturated fatty acids and which does not form volatile fatty acids in the intestinal tract.

Mull-Soy is a liquid, palatable, homogenized (vacuum packed) food —easy to take, easy to prescribe. Available in drugstores in 15½ fl. oz. tins.

*Hill, L. W.: New England J. Med. 242:288, 1950

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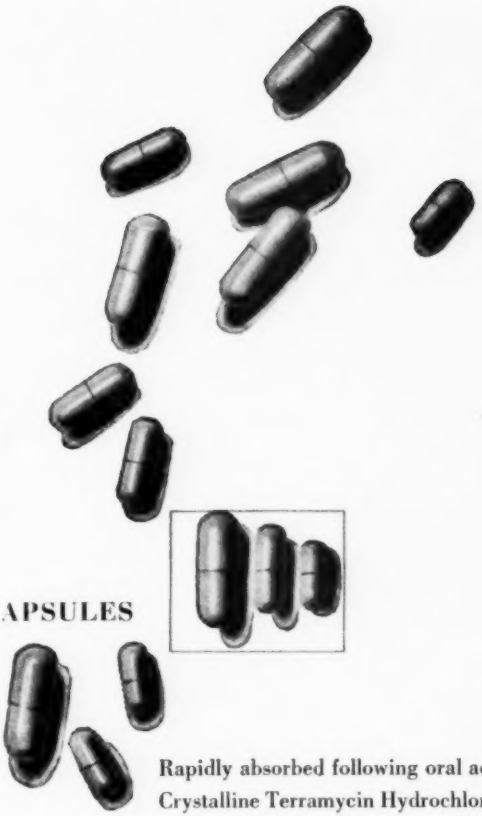

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100 mg., bottles of 25 and 100;
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FEBRUARY 7

1. RECENT ADVANCES IN THE MANAGEMENT OF PULMONARY TUBERCULOSIS—Burns J. Amberson, *Professor of Medicine, College of Physicians and Surgeons, Columbia University; Visiting Professor in charge of Chest Service, Bellevue Hospital.*

FEBRUARY 14

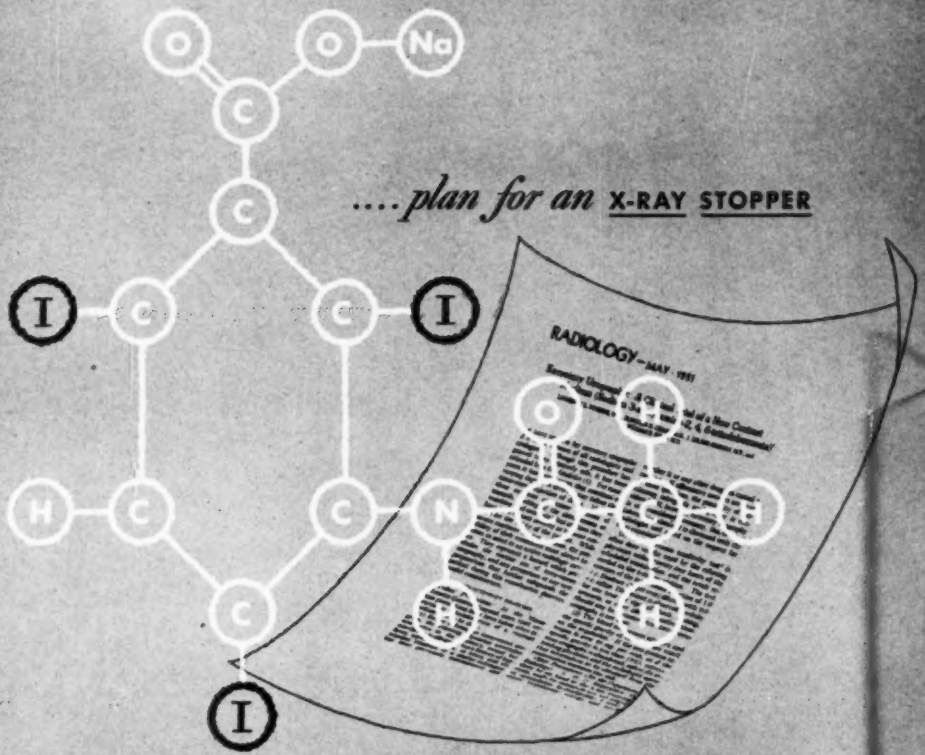
2. RECENT ADVANCES IN THE KNOWLEDGE OF NON-TUBERCULOUS PULMONARY DISEASES—Alvan L. Barach, *Associate Professor of Clinical Medicine, Columbia University, College of Physicians and Surgeons; Associate Attending Physician, Presbyterian Hospital.*

FEBRUARY 21

3. EXTERNAL DISEASES OF THE EYE AND THEIR TREATMENT—Walter S. Atkinson, *Associate Clinical Professor of Ophthalmology, New York University Post-Graduate Medical School; Ophthalmologist, House of the Good Samaritan, Watertown, New York.*

FEBRUARY 28

4. CORONARY DISEASE: CLINICAL-PATHOLOGIC CORRELATIONS AND PHYSIOLOGY—Herman L. Blumgart, *Physician-in-Chief, Beth Israel Hospital, Boston, and Professor of Medicine, Harvard Medical School.*



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Editorial: J.A.M.A. *135*:576, Nov. 1, 1947.

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Griggs, D. E., and Johns, V. J.: California Med. *69*:133, Aug. 1948.

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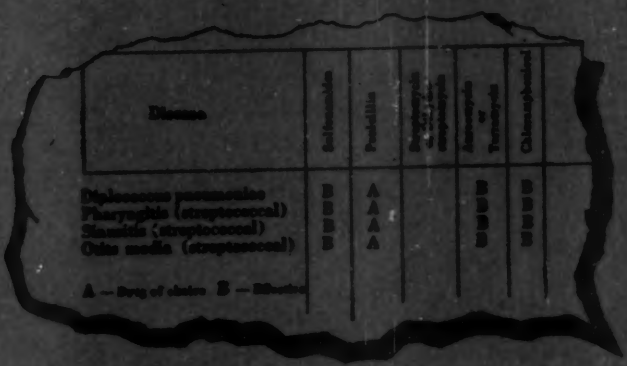
Disease
Penicillin
Chloramphenicol
Diplococcus pneumoniae B A B B
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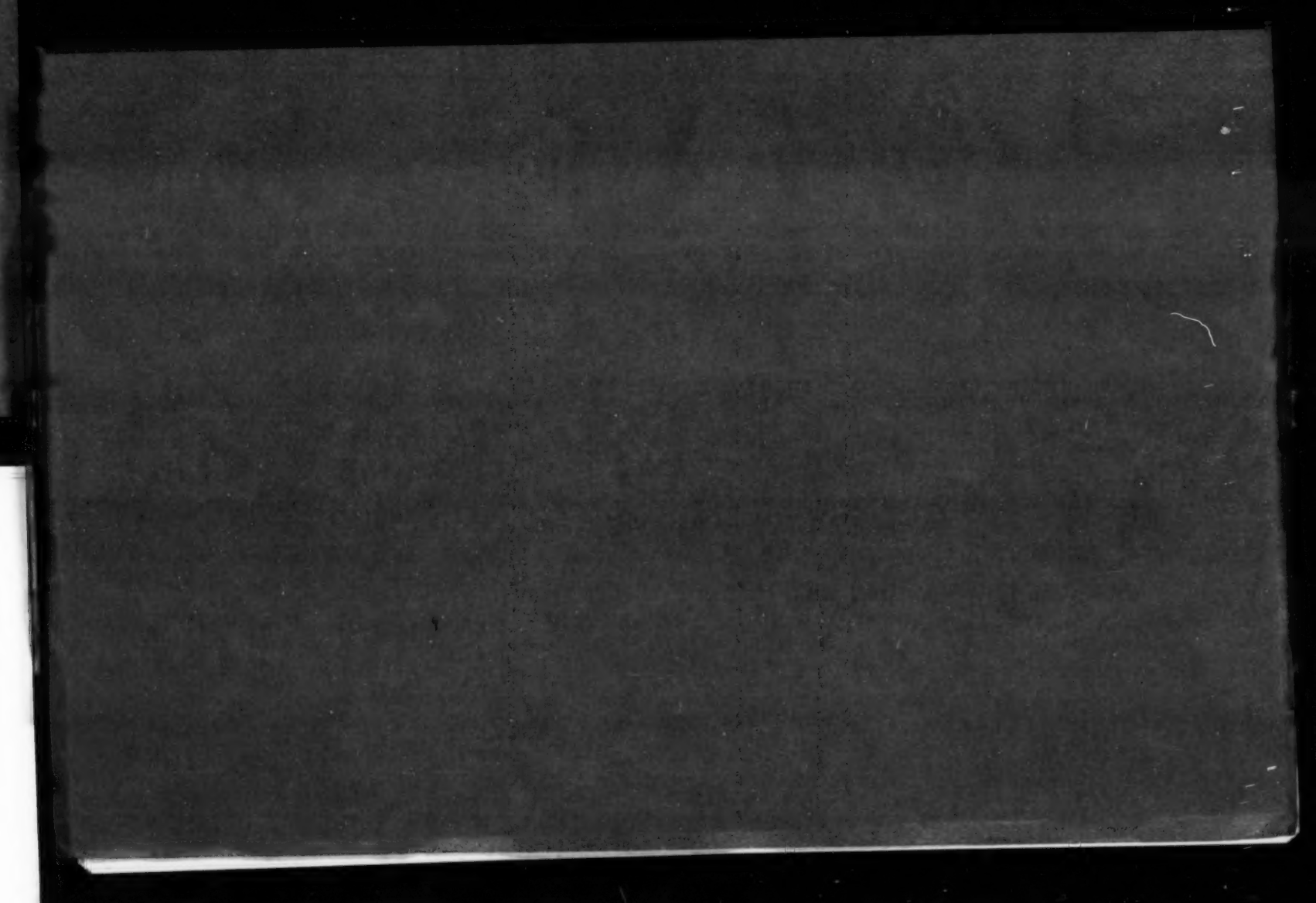
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